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=> d his ful

     (FILE 'HOME' ENTERED AT 14:30:47 ON 15 MAY 2006)

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L2            STR
L3            STR
L5        30914 SEA SSS FUL L2 AND L3

     FILE 'HCAPLUS' ENTERED AT 14:40:25 ON 15 MAY 2006
L7        12423 SEA ABB=ON  PLU=ON  L5
L9       327157 SEA ABB=ON  PLU=ON  CONDENSATION REACT?/CV OR CONDENSATION
L11     1181659 SEA ABB=ON  PLU=ON  REDUCT?/CV OR REDUCT? OR RDX
L13        1671 SEA ABB=ON  PLU=ON  L7(L)SPN/RL
L14         130 SEA ABB=ON  PLU=ON  L13 AND L9
L15          16 SEA ABB=ON  PLU=ON  L14 AND L11
L16       10276 SEA ABB=ON  PLU=ON  L7 AND PD=<OCTOBER 1, 2003
L17          16 SEA ABB=ON  PLU=ON  L16 AND L15
               D STAT QUE L17
               D IBIB ABS HITSTR L17 1-16
L18         214 SEA ABB=ON  PLU=ON  ("OFFORD R"/AU OR "OFFORD R E"/AU) OR
               ("OFFORD ROBIN"/AU OR "OFFORD ROBIN E"/AU OR "OFFORD ROBIN
               EWART"/AU)
L19         250 SEA ABB=ON  PLU=ON  ("ROSE K"/AU OR "ROSE K A"/AU) OR ("ROSE
               KEITH"/AU OR "ROSE KEITH A"/AU OR "ROSE KEITH ALLAN"/AU)
L20          69 SEA ABB=ON  PLU=ON  L18 AND L19
L21           0 SEA ABB=ON  PLU=ON  L20 AND L7
L22           7 SEA ABB=ON  PLU=ON  (L7 AND (L18 OR L19)) NOT (L20 OR L17)
L23          76 SEA ABB=ON  PLU=ON  L20 OR L21 OR L22
               D STAT QUE L23 NOS
               D IBIB ABS HITSTR L23 1-76

     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   14 MAY 2006  HIGHEST RN 884198-07-6
     DICTIONARY FILE UPDATES:  14 MAY 2006  HIGHEST RN 884198-07-6

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.

     ************************************************************
     *                                                          *
     * The CA roles and document type information have been removed from *
     * the IDE default display format and the ED field has been added,   *
     * effective March 20, 2005.  A new display format, IDERL, is now    *
     * available and contains the CA role and document type information. *
     *                                                          *
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     Structure search iteration limits have been increased.  See HELP SLIMITS
     for details.
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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE HCAPLUS

FILE COVERS 1907 - 15 May 2006 VOL 144 ISS 21
FILE LAST UPDATED: 14 May 2006 (20060514/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> d stat que l17
L2                STR
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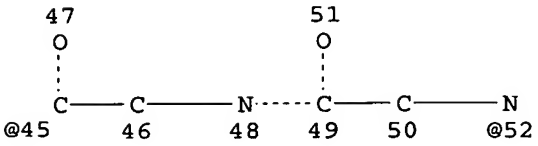

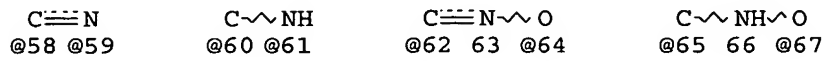


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NUMBER OF NODES IS  23

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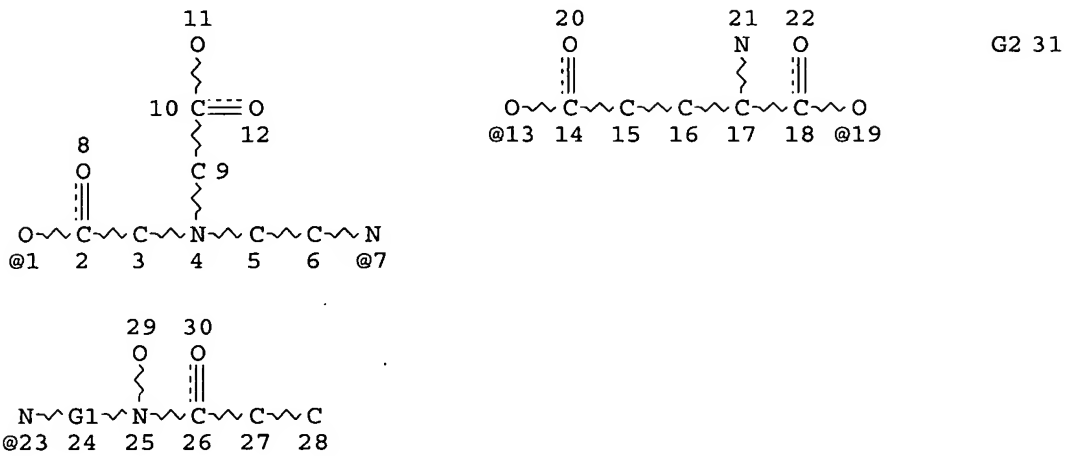


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L9        327157 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CONDENSATION REACT?/CV OR
                 CONDENSATION
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L11     1181659 SEA FILE=HCAPLUS ABB=ON  PLU=ON  REDUCT?/CV OR REDUCT? OR RDX
L13        1671 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7(L)SPN/RL
L14         130 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 AND L9
L15          16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 AND L11
L16       10276 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND PD=<OCTOBER 1, 2003
L17          16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND L15


=> d ibib abs hitstr l17 1-16

L17  ANSWER 1 OF 16  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         1993:255354  HCAPLUS
DOCUMENT NUMBER:          118:255354
TITLE:                    Somatostatin analogues containing chelating groups and
                          their radiolabeled compositions
INVENTOR(S):              Albert, Rainer; Krenning, Eric Paul; Lamberts, Steven
                          Willem; Pless, Janos
PATENT ASSIGNEE(S):       Sandoz Ltd., Switz.; Sandoz-Patent-G.m.b.H.
SOURCE:                   Eur. Pat. Appl., 19 pp.
                          CODEN: EPXXDW
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

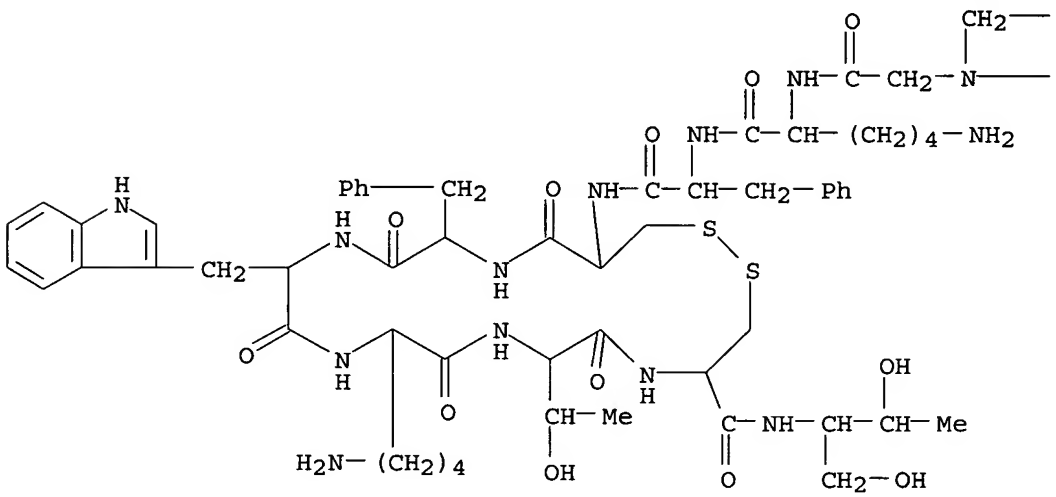
     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     EP 515313             A2    19921125    EP 1992-810381          19920520 <--
     EP 515313             A3    19940413
     EP 515313             B1    20000809
         R:  BE, CH, DE, FR, GB, IT, LI, NL
     CA 2069154            AA    19921124    CA 1992-2069154         19920521 <--
     CA 2069154            C     20030107
     JP 05163297           A2    19930629    JP 1992-130676          19920522 <--
     JP 3397338            B2    20030414
     US 5776894            A     19980707    US 1995-479052          19950606 <--
PRIORITY APPLN. INFO.:                       GB 1991-11199       A   19910523
                                             GB 1988-28364       A   19881205
                                             GB 1989-16115       A   19890713
                                             GB 1989-16761       A   19890721
                                             US 1989-445815      B2  19891204
                                             US 1991-709868      B1  19910603
                                             US 1993-34336       B1  19930322
                                             US 1994-328296      B1  19941024
OTHER SOURCE(S):          MARPAT 118:255354
GI   For diagram(s), see printed CA Issue.
AB   The preparation of cyclic or linear somatostatin peptide analogs
     X-A-Cys(Y1)-B-C-Lys-E-Cys(Y2)-G [X = p-R3CH2C6H4NHCS, Q1,
     [AcN(OH)(CH2)5NHCO(CH2)2]2CON(OH)(CH2)5NHY, Q1-Lys, H-Lys(Q1), D1-Lys(Q1),
     (MO2CCH2)2NCH2CH2N(CH2CO2M)CH2CH[N(CH2CO2M)2], Q1 =
     (MO2CCH2)2CH2CH2N(CH2CO2M)CH2CH2N(CH2CO2M)CH2CO, M = H, pharmaceutically
     acceptable cation equivalent, R3 = CH(CH2NHCMe2CMe:NOH)2, Q1, Q2, Q3, n = 0,
     1, Y = divalent spacer group; A = D-Phe, D-Trp, D-(β-naphthyl)alanine
     (D-β-Nal); B = optionally halo- or hydroxy-ring substituted
     β-Nal, Thr; C = D-Trp, Trp; E = Thr, Ser, Val; G = NHCHR4CH2OR5,
     NHCHR4CONH2, R4 = Thr, β-Nal, Trp side chain, R5 = H, physiol.
     hydrolyzable ester group; Y1Y2 = bond, Y1 = Y2 = H] containing specific
     chelating groups in free or salt forms for complexation with β-,
     γ-, or positron-emitting elements for use as radiopharmaceuticals is
     described.  Thus, ligand I (n = 0, M = H, Thr-ol = L-threoninol) was
```

prepared by addition of isothiocyanate p-Q2CH2C6H4NCS to the corresponding lysine-protected peptide alc., followed by deprotection with piperidine. I was complexed with 90Y to give the corresponding radionucleotide complex.

IT **147790-83-8P 147790-85-0P**
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation of, as chelating agent for radiopharmaceuticals)

RN 147790-83-8 HCAPLUS
CN L-Cysteinamide, N-[2-[[2-[bis(carboxymethyl)amino]ethyl](carboxymethyl)amino]ethyl]-N-(carboxymethyl)glycyl-L-lysyl-D-phenylalanyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-N-[2-hydroxy-1-(hydroxymethyl)propyl]-, cyclic (4→9)-disulfide, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

PAGE 1-A



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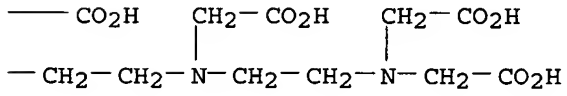
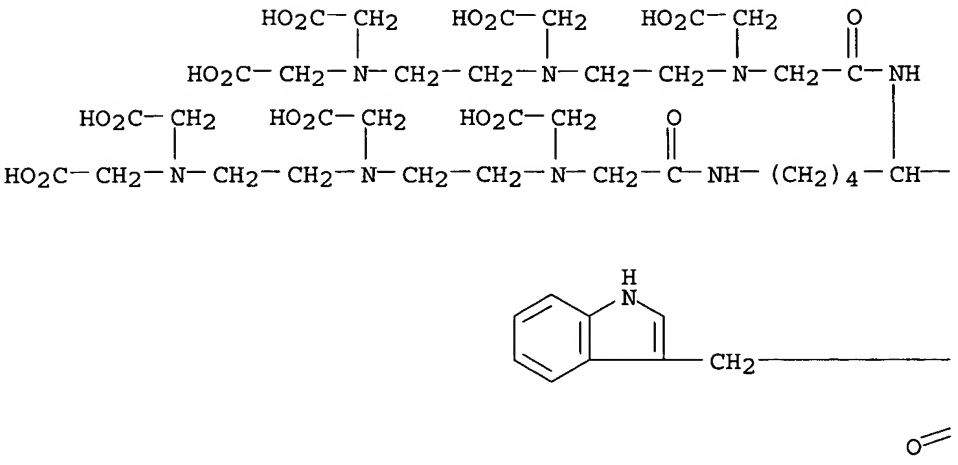


RN 147790-85-0 HCAPLUS
CN L-Cysteinamide, N-[2-[[2-[bis(carboxymethyl)amino]ethyl](carboxymethyl)amino]ethyl]-N-(carboxymethyl)glycyl-N6-[N-[2-[[2-[bis(carboxymethyl)amino]ethyl](carboxymethyl)amino]ethyl]-N-(carboxymethyl)glycyl]-L-lysyl-D-phenylalanyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-N-[2-hydroxy-1-(hydroxymethyl)propyl]-, cyclic (4→9)-disulfide, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

PAGE 1-A



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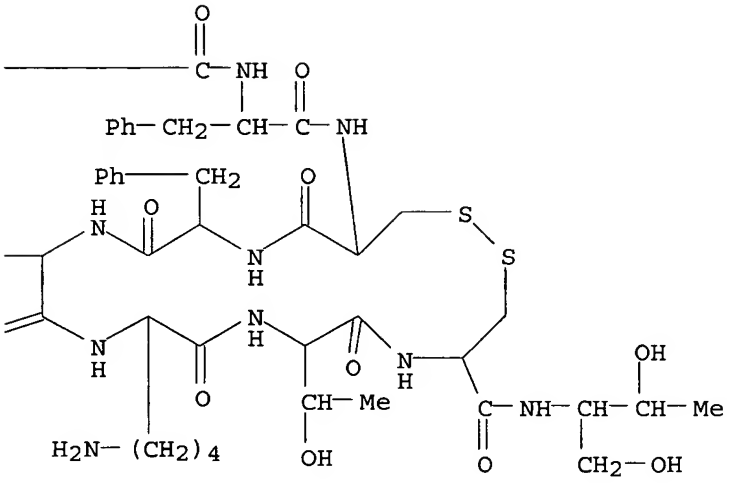


L17 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:612921 HCAPLUS
DOCUMENT NUMBER: 117:212921
TITLE: Synthesis of segments of the GnRH-associated peptide
AUTHOR(S): Somlai, Csaba; Koenig, Wolfgang; Knolle, Jochen
CORPORATE SOURCE: Dep. Med. Chem., Albert Szent-Gyorgyi Med. Univ., Szeged, H-6720, Hung.
SOURCE: Liebigs Annalen der Chemie (**1992**), (10), 1055-61
CODEN: LACHDL; ISSN: 0170-2041
DOCUMENT TYPE: Journal

LANGUAGE: English

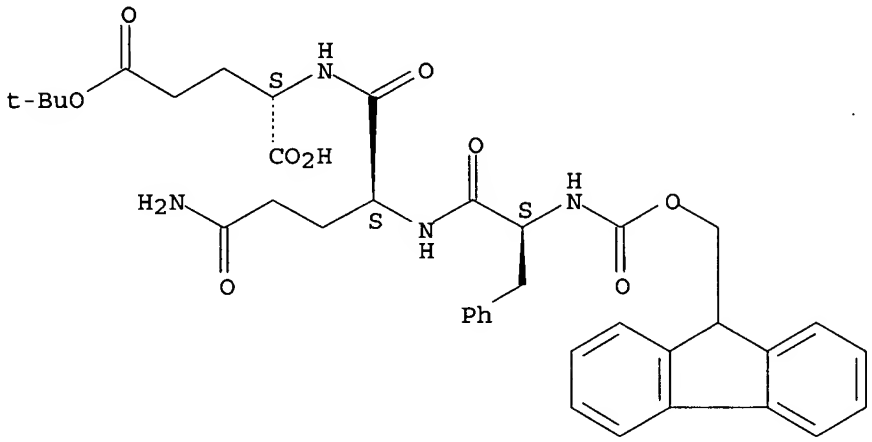
AB The 56 amino acid containing GnRH-associated peptide (GAP) may be prepared by a combination of fragment **condensation** and solid-phase peptide synthesis (SPPS). The solution-phase synthesis of 9 fragments is described. Furthermore, the selective cleavage of benzyl esters by catalytic hydrogenation in the presence of the 9-fluorenylmethyloxycarbonyl (Fmoc) protecting group is reported. The C-terminal 15 amino acid containing fragment of GAP was synthesized by SPPS.

IT **143038-32-8P 143038-35-1P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and deblocking of, with ethyldiisopropylamine)

RN 143038-32-8 HCAPLUS

CN L-Glutamic acid, N-[N2-[N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-phenylalanyl]-L-glutaminyl]-, 5-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

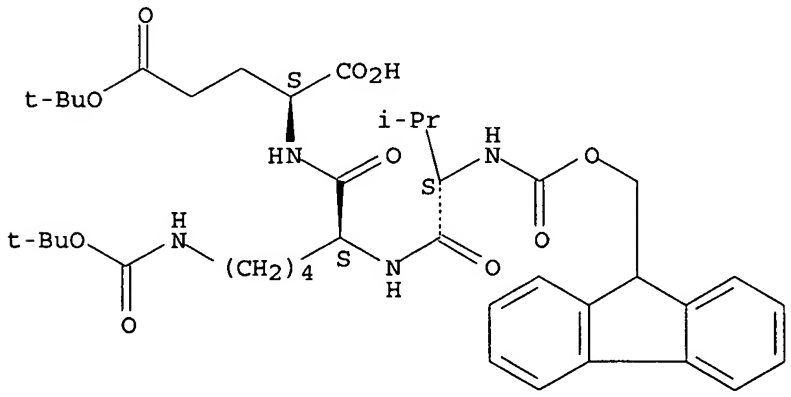
Absolute stereochemistry.



RN 143038-35-1 HCAPLUS

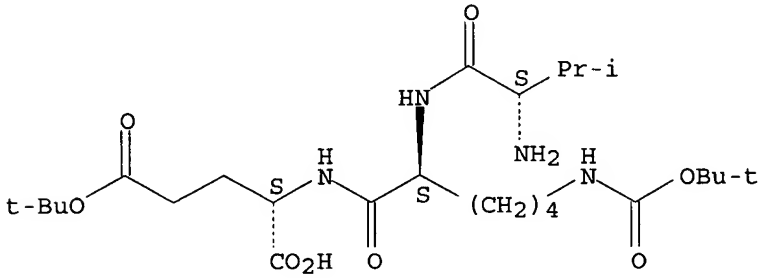
CN L-Glutamic acid, N-[N6-[(1,1-dimethylethoxy)carbonyl]-N2-[N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-valyl]-L-lysyl]-, 5-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



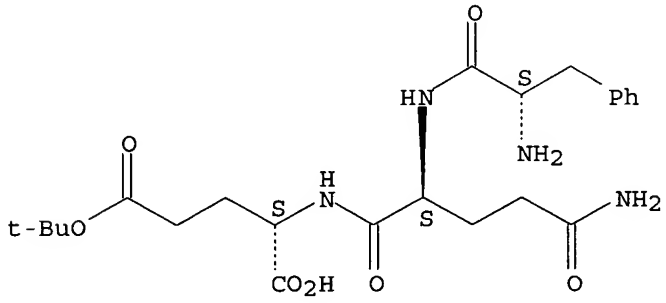
IT **143063-36-9P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with isoleucine active ester in preparation
of gonadoliberin releasing hormone fragment)
RN 143063-36-9 HCAPLUS
CN L-Glutamic acid, N-[N6-[(1,1-dimethylethoxy)carbonyl]-N2-L-valyl-L-lysyl]-, 5-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



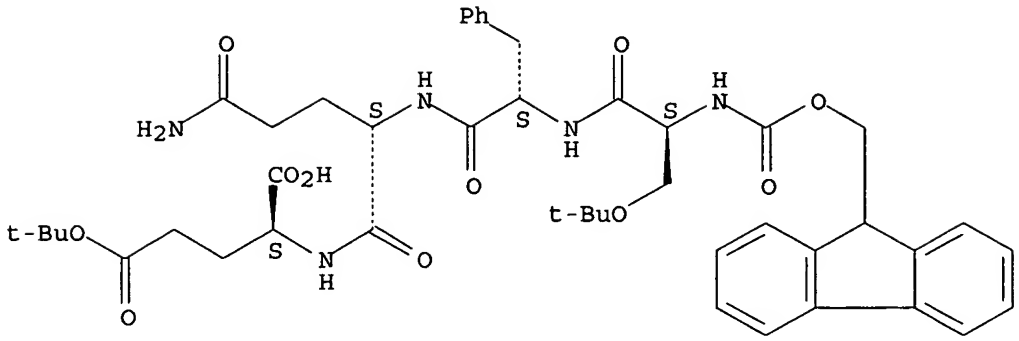
IT **143038-33-9P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with serine active ester in preparation of
gonadoliberin releasing hormone fragment)
RN 143038-33-9 HCAPLUS
CN L-Glutamic acid, N-(N2-L-phenylalanyl-L-glutaminyl)-, 5-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



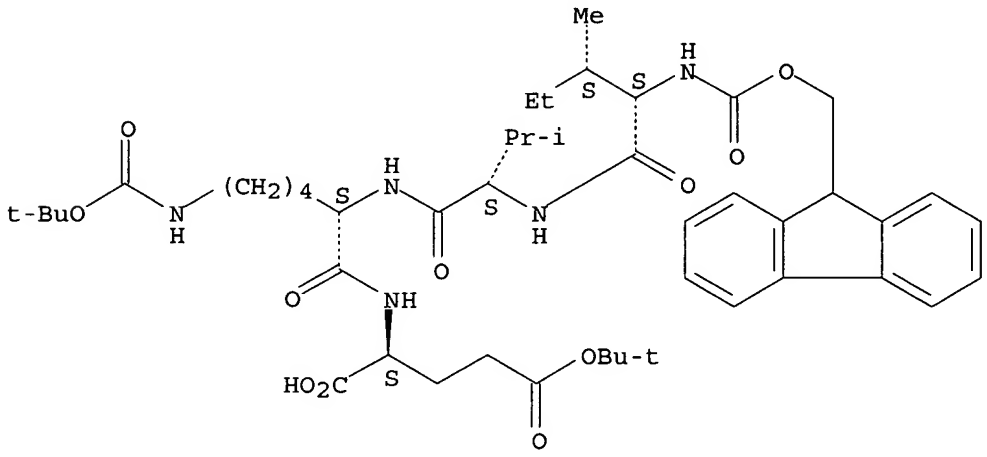
IT **143038-19-1P 143063-31-4P**
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation of, as intermediate in preparation of gonadoliberin releasing hormone)
RN 143038-19-1 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[O-(1,1-dimethylethyl)-N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-seryl]-L-phenylalanyl]-L-glutaminyl]-, 5-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 143063-31-4 HCAPLUS
CN L-Glutamic acid, N-[N6-[(1,1-dimethylethoxy)carbonyl]-N2-[N-[N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-isoleucyl]-L-valyl]-L-lysyl]-, 5-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:450264 HCAPLUS
DOCUMENT NUMBER: 115:50264
TITLE: Synthesis of peptides containing unnatural, metal-ligating residues: aminodiacetic acid as a peptide side chain
AUTHOR(S): Ruan, Fuqiang; Chen, Yanqiu; Itoh, Katsumi; Sasaki, Tomikazu; Hopkins, Paul B.
CORPORATE SOURCE: Dep. Chem., Univ. Washington, Seattle, WA, 98195, USA
SOURCE: Journal of Organic Chemistry (1991), 56(14), 4347-54
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 115:50264
AB Peptides possessing a pair of residues separated by one turn in the α-helical conformation and potentially capable of ligating a single metal ion in aqueous solution were designed. The resulting crossink should shift the random coil/α-helix equilibrium toward the α-helix. The

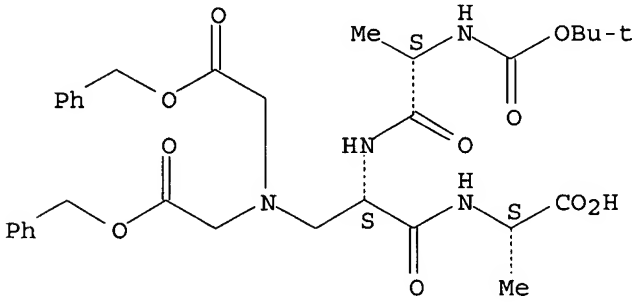
syntheses of 10 peptides Ac-Ada-Alam-Ada-(Ada4-Glu-Lys)n-NH2 [Ada = L-NHCH[(CH2)xN(CH2CO2H)2]CO; n = 1-3, x = 1, m = 3; n = 3, x = 1-4, m = 2, 3] are described using tert-butoxycarbonyl chemical on p-methylbenzhydrylamine resin. The aminodiacetic acid bearing residues were incorporated with side chains protected as the dibenzyl esters. To avoid side reactions, residues Ada (x = 1, 2) were incorporated by a block approach. Peptides were confirmed by observation of the predicted parent ions in the fast-atom-bombardment mass spectra.

IT **134653-46-6P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling reactions of)

RN 134653-46-6 HCAPLUS

CN L-Alanine, N-[3-[bis[2-oxo-2-(phenylmethoxy)ethyl]amino]-N-[N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl]-L-alanyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

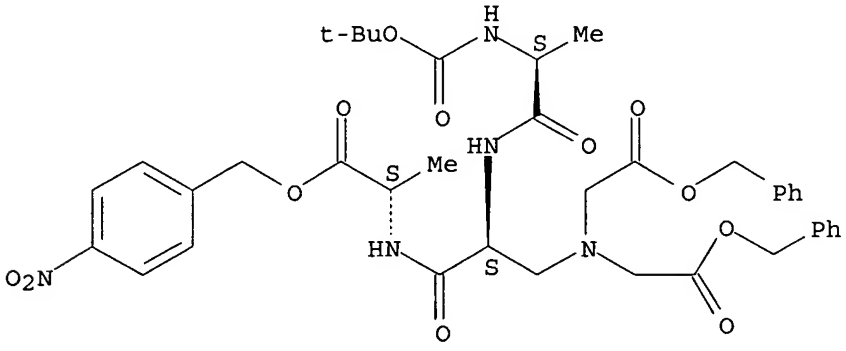


IT **134653-41-1P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and **reductive** deesterification of)

RN 134653-41-1 HCAPLUS

CN L-Alanine, N-[3-[bis[2-oxo-2-(phenylmethoxy)ethyl]amino]-N-[N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl]-L-alanyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

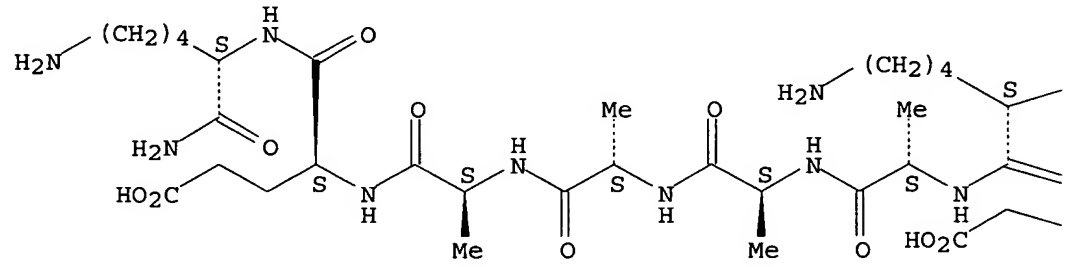


IT **130883-81-7P 130883-85-1P 130903-40-1P**
134653-27-3P
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation of)

RN 130883-81-7 HCAPLUS
CN L-Lysinamide, N-acetyl-3-[bis(carboxymethyl)amino]-L-alanyl-L-alanyl-L-alanyl-3-[bis(carboxymethyl)amino]-L-alanyl-L-alanyl-L-alanyl-L-alanyl-L-alanyl-L-α-glutamyl-L-lysyl-L-alanyl-L-alanyl-L-alanyl-L-alanyl-L-α-glutamyl-L-lysyl-L-alanyl-L-alanyl-L-alanyl-L-alanyl-L-α-glutamyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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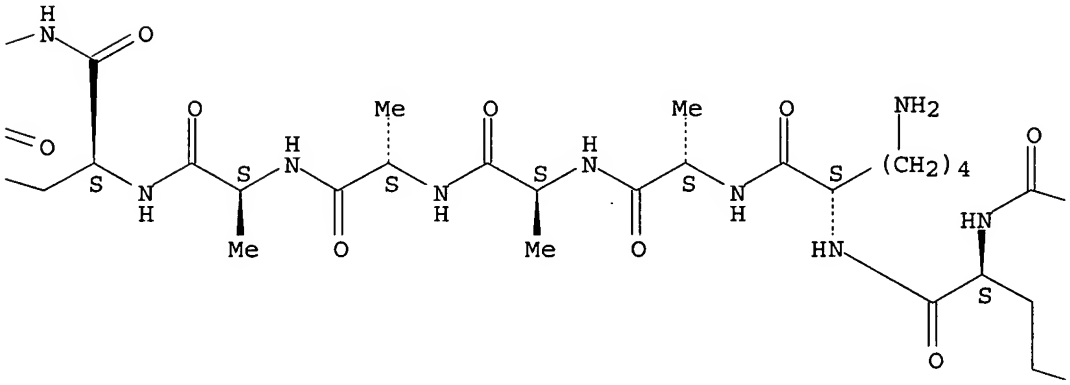

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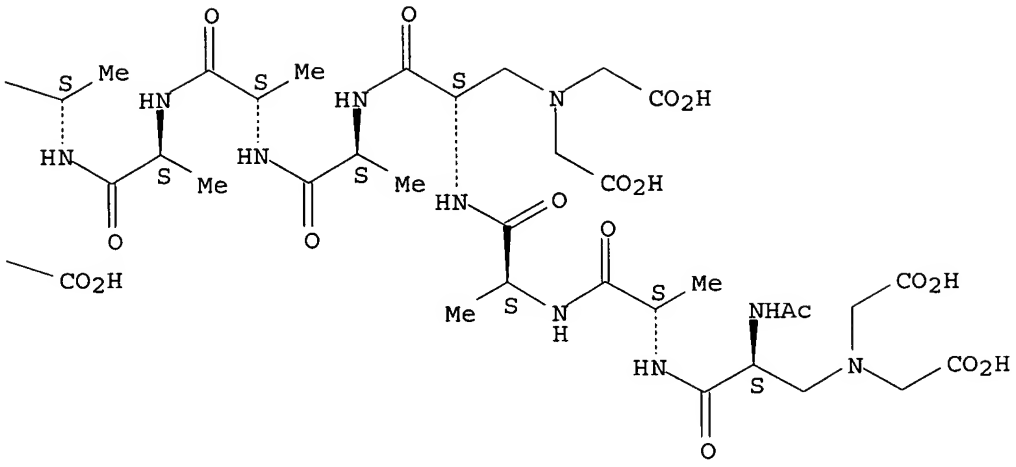

RN 130883-85-1 HCAPLUS
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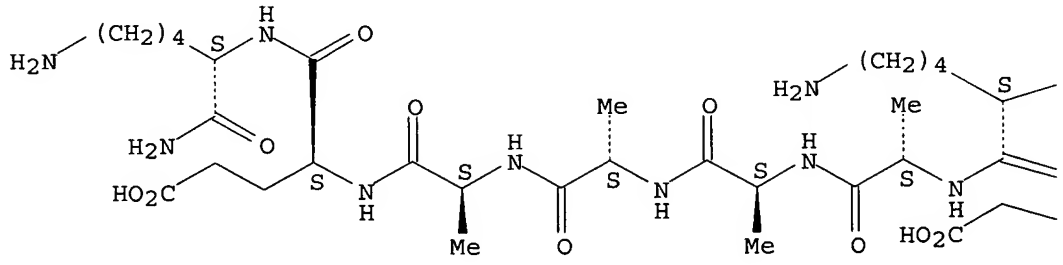
Absolute stereochemistry.

PAGE 1-A



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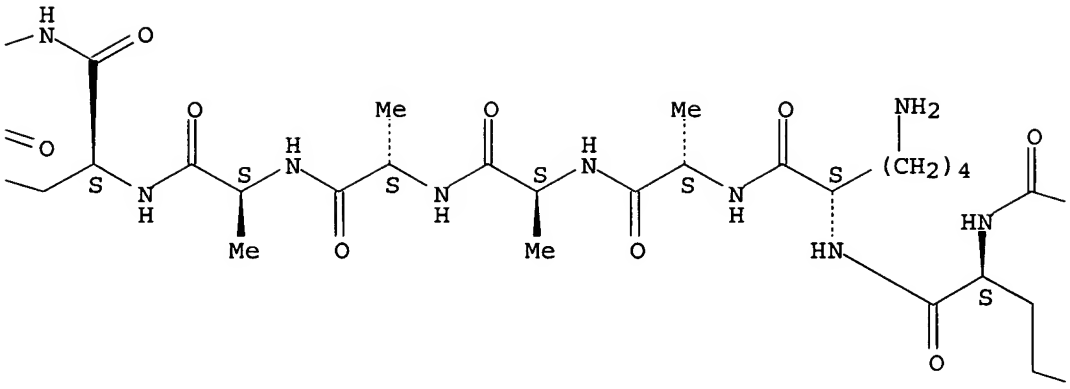

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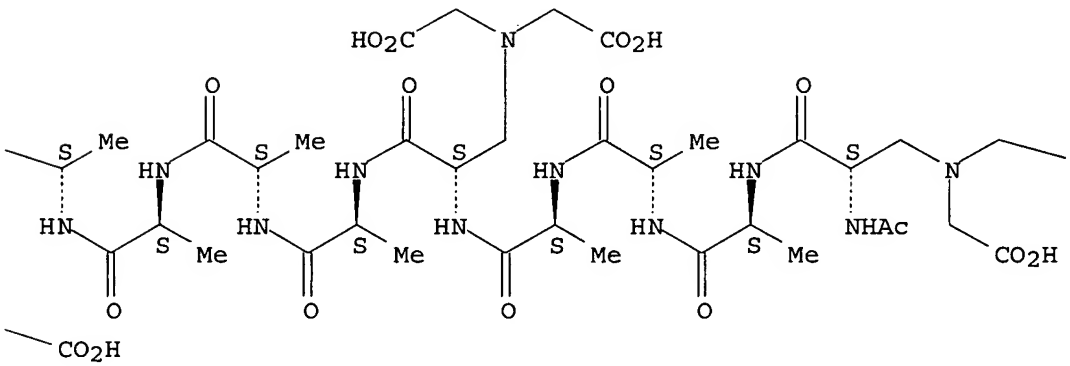
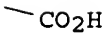


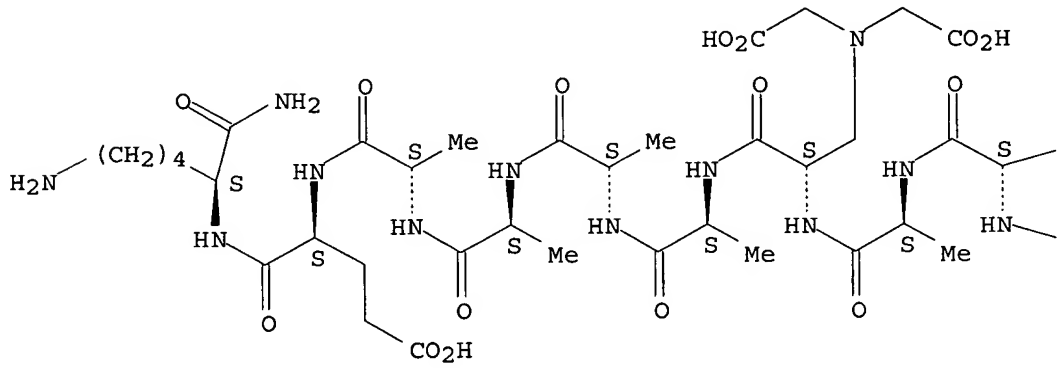
PAGE 1-D



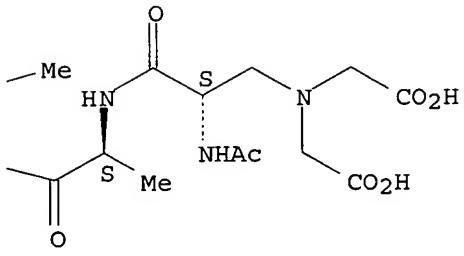
RN 130903-40-1 HCAPLUS
CN L-Lysinamide, N-acetyl-3-[bis(carboxymethyl)amino]-L-alanyl-L-alanyl-L-alanyl-L-alanyl-3-[bis(carboxymethyl)amino]-L-alanyl-L-alanyl-L-alanyl-L-alanyl-L-α-glutamyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



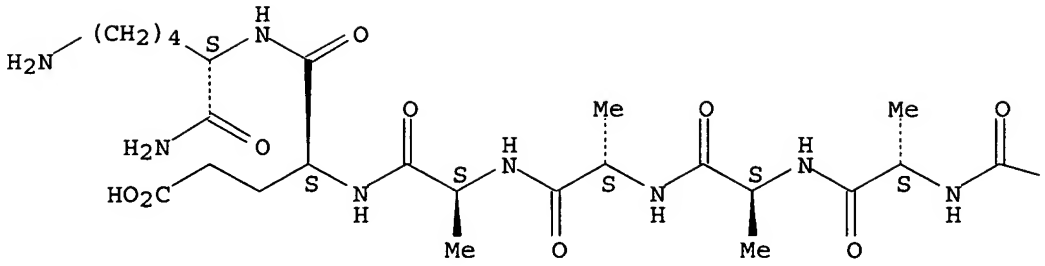
PAGE 1-B



RN 134653-27-3 HCAPLUS
CN L-Lysinamide, N-acetyl-3-[bis(carboxymethyl)amino]-L-alanyl-L-alanyl-L-alanyl-L-alanyl-3-[bis(carboxymethyl)amino]-L-alanyl-L-alanyl-L-alanyl-L-alanyl-L-α-glutamyl-L-lysyl-L-alanyl-L-alanyl-L-alanyl-L-alanyl-L-α-glutamyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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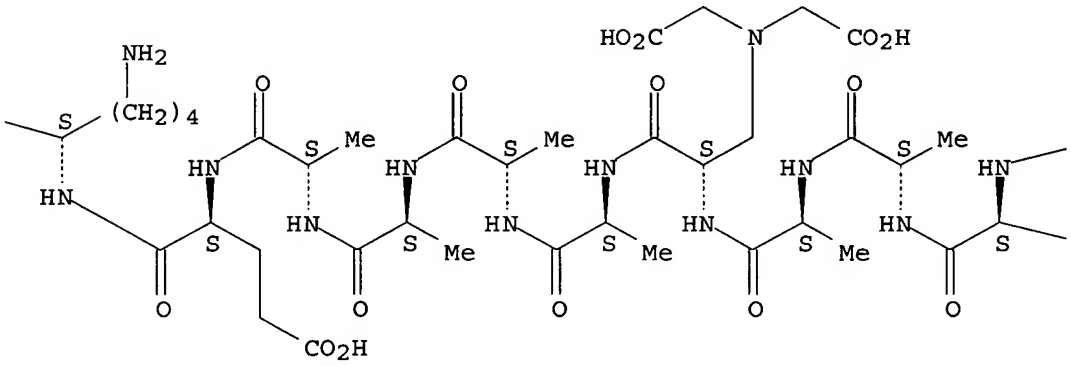
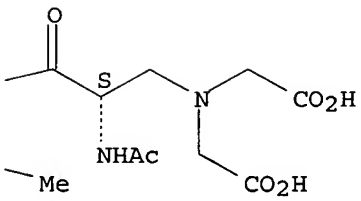


PAGE 1-C



L17 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:186058 HCAPLUS
DOCUMENT NUMBER: 114:186058
TITLE: Evaluation of the oxime resin based segment synthesis-**condensation** approach using RNase T1 as a model synthetic target

AUTHOR(S): Sasaki, Tomikazu; Findeis, Mark A.; Kaiser, Emil Thomas
CORPORATE SOURCE: Lab. Bioorg. Chem. Biochem., Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Journal of Organic Chemistry (**1991**), 56(9), 3159-68
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The p-nitrobenzophenone oxime resin has been used as a support for the synthesis of a series of protected peptides based on the sequence of the guanyloribonuclease RNase T1. As a further test of the utility of oxime resin these protected peptides have been assembled by a convergent strategy using a combination of solid- and solution-phase coupling steps. An analog in which 11 out of 17 residues in an α-helical region of the enzyme have been changed was also synthesized by changing three of the protected peptides in the synthesis of the native sequence enzyme. Following deprotection with the low-high HF method, the resulting synthetic enzymes had very low specific activity (<0.1%). The appropriate use of oxime resin in peptide synthesis is discussed.

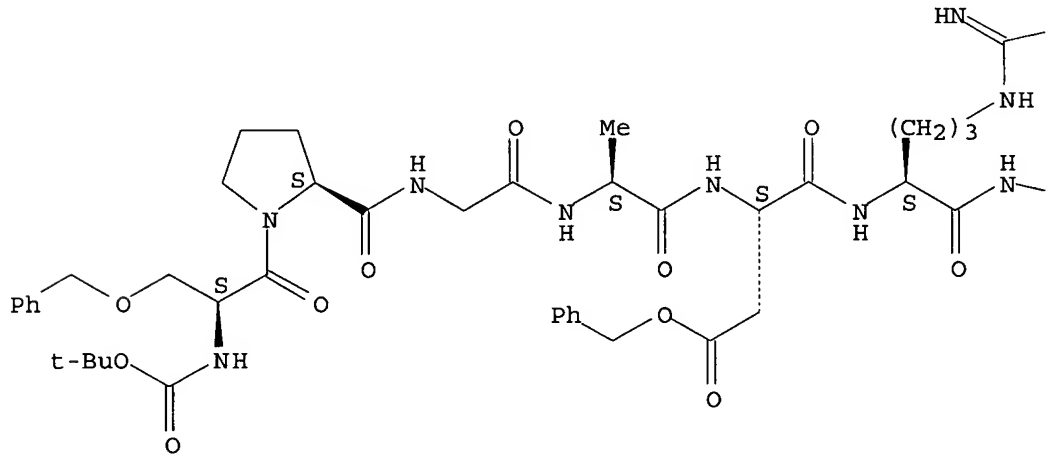
IT **132376-48-8P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with guanyloribonuclease fragment)

RN 132376-48-8 HCAPLUS

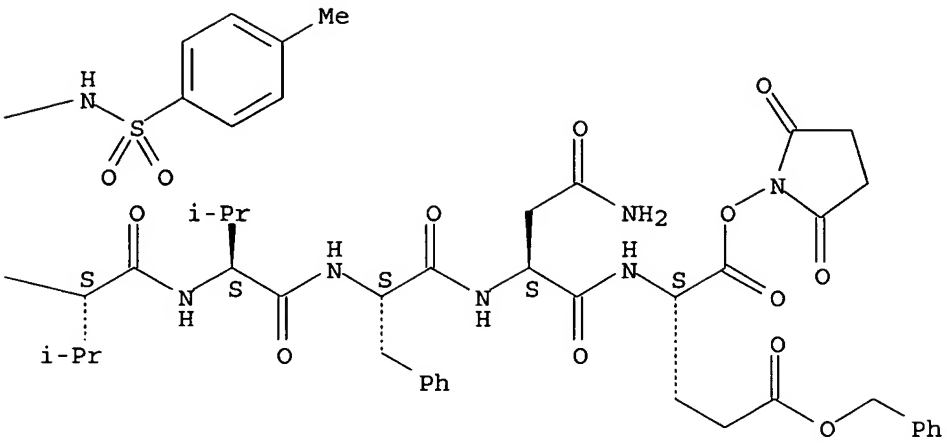
CN 2,5-Pyrrolidinedione, 1-[[N-[N2-[N-[N-[N-[N2-[N-[N-[N-[1-[N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl]-L-prolyl]glycyl]-L-alanyl]-L-α-asparty l]-N5-[imino[[(4-methylphenyl)sulfonyl]amino]meth yl]-L-ornithyl]-L-valyl]-L-valyl]-L-phenylalanyl]-L-asparaginyl]-L-α-glutamyl]oxy]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

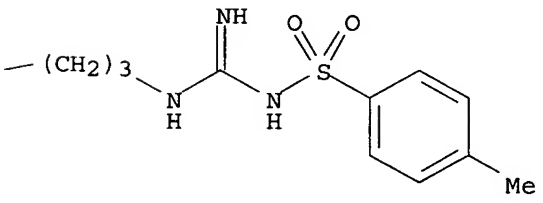


IT **132376-37-5P 132376-39-7P**
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation of, by solid-phase method on oxime resin and coupling reactions of, guanyloribonuclease derivs. from)
RN 132376-37-5 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[N-[N-[N2-[N-[N-[N-[1-[N-[(1,1-dimethylethoxy)carbonyl]-O-(phenylmethyl)-L-seryl]-L-prolyl]glycyl]-L-alanyl]-L-α-asparty l]-N5-[imino[[(4-methylphenyl)sulfonyl]amino]meth yl]-L-ornithyl]-L-valyl]-L-valyl]-L-phenylalanyl]-L-asparaginyl]-, 4,5-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

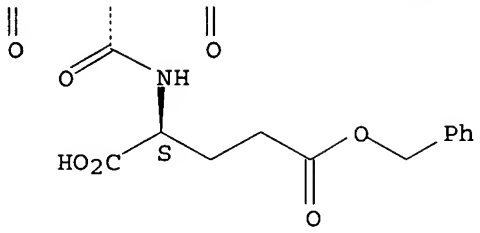
Absolute stereochemistry.

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

PAGE 1-B

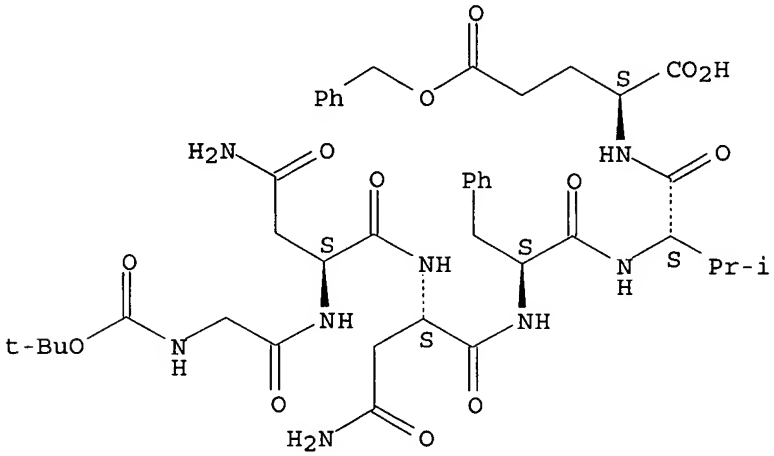


PAGE 2-A



RN 132376-39-7 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N2-[N2-[N-[(1,1-dimethylethoxy)carbonyl]glycyl]-L-asparaginyl]-L-asparaginyl]-L-phenylalanyl]-L-valyl]-, 5-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:173764 HCAPLUS
DOCUMENT NUMBER: 110:173764
TITLE: Preparation and testing of statine-containing peptides as renin inhibitors
INVENTOR(S): Bindra, Jasit S.; Kleinman, Edward F.; Rosati, Robert L.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 16 pp. Cont.-in-part of U.S. Ser. No. 763,768, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4749687	A	19880607	US 1986-839010	19860310 <--
CA 1254699	A1	19890523	CA 1985-476191	19850311 <--
PRIORITY APPLN. INFO.:			US 1984-588279 A1	19840312
			CA 1985-476191 A	19850311

US 1985-763768 A2 19850808

OTHER SOURCE(S): MARPAT 110:173764

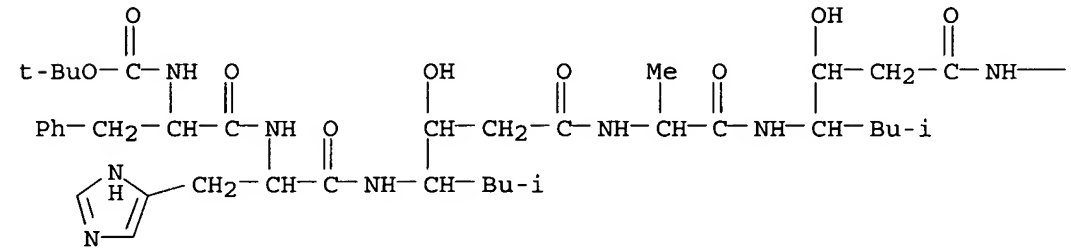
AB RWW1NHCHR2CHR3CH2COR1 [I; R = H, acyl, (protected) Pro, pyroglutamyl; W = Phe, His, Leu, Tyr, 1-naphthylalanyl; W1 = Phe, His, Leu, Tyr, Nle; the N of the WW1 peptide link may be substituted by C1-4 alkyl when W = Phe and W1 = His; R2 = H, C1-6 alkyl, Ph, C4-7 cycloalkyl, C7-9 phenylalkyl, C5-10 cycloalkyl(alkylene); R3 = OH, amino, acylamino, alkoxy, alkoxycarbonyl; R1 = amino, C1-4 alkoxy, 4-benzylpiperazin-1-yl, 1,2,3,4-tetrahydroquinolin-1-yl, A-E-B, etc.; A = Lys, Pro, Ile; E = Phe, Gly, Ala, Val, Ile, Lys, Orn, Arg, Asp, etc.; B = OH, alkoxy, amino, glutamyl, etc.] and their salts were prepared as renin inhibitors. BOC-Phe-His-Sta-Ile-Sta-OH (Sta = 4S-amino-3S-hydroxy-6-methylheptanoyl), prepared by the solution phase method, inhibited renin with an IC50 of <4 μmol/L.

IT **100512-31-0P 100512-35-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; BIOL (Biological study); PREP (Preparation)
(preparation of, as renin inhibitor)

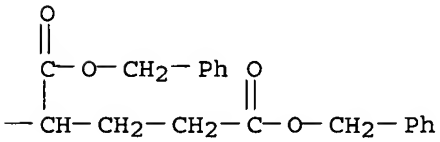
RN 100512-31-0 HCAPLUS

CN L-Histidinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[2,10-dihydroxy-6-methyl-1,9-bis(2-methylpropyl)-4,7,12,17-tetraoxo-19-phenyl-14-[(phenylmethoxy)carbonyl]-18-oxa-5,8,13-triazanonadec-1-yl]-, [1S-(1R*,2R*,6R*,9R*,10R*,14R*)]- (9CI) (CA INDEX NAME)

PAGE 1-A



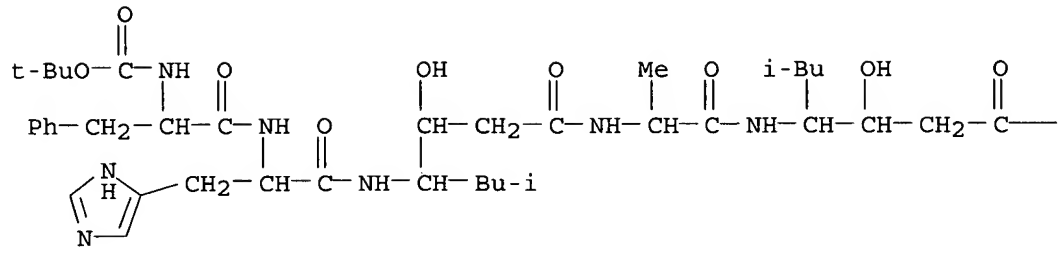
PAGE 1-B



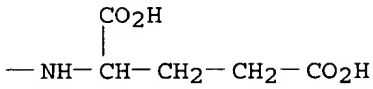
RN 100512-35-4 HCAPLUS

CN L-Histidinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[4-[[2-[[4-[(1,3-dicarboxypropyl)amino]-2-hydroxy-1-(2-methylpropyl)-4-oxobutyl]amino]-1-methyl-2-oxoethyl]amino]-2-hydroxy-1-(2-methylpropyl)-4-oxobutyl]-, stereoisomer (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



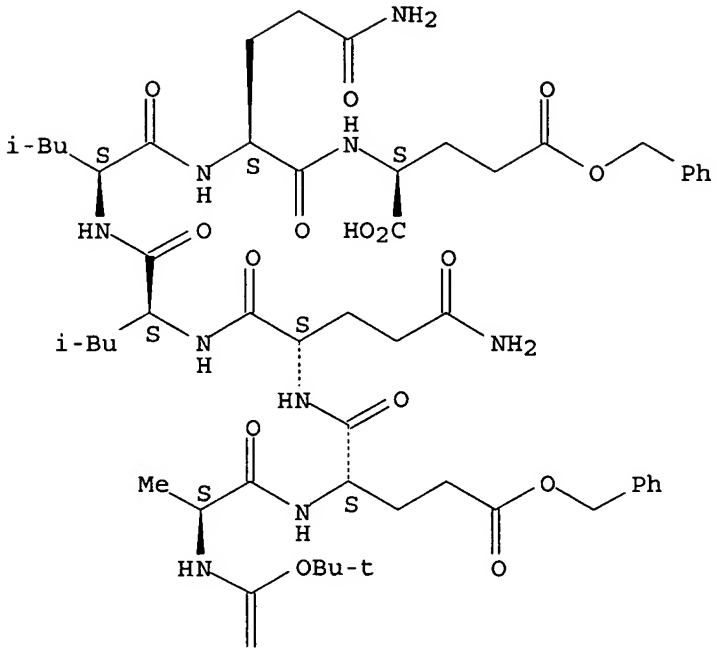
L17 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:71753 HCAPLUS
DOCUMENT NUMBER: 110:71753
TITLE: Helichrome: synthesis and enzymic activity of a designed hemeprotein
AUTHOR(S): Sasaki, Tomikazu; Kaiser, Emil T.
CORPORATE SOURCE: Lab. Bioorg. Chem. Biochem., Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Journal of the American Chemical Society (**1989**), 111(1), 380-1
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A hemoprotein model containing synthetic peptides was prepared to create a protein-like catalytic domain by using new principles of protein design. A 15-residue peptide was designed to form an amphiphilic α-helix and synthesized via the segment synthesis-**condensation** approach. This peptide was covalently attached to each of the 4 carboxyl groups of coproporphyrin I to allow folding into a 4-helix-bundle type conformation. The resulting mol. (helichrome) was found to be monomeric in buffer solution Its CD spectrum (.apprx.70% α-helix in buffer solution) and fluorescence spectrum were in agreement with the expected structure. The helichrome showed aniline hydroxylase activity with kcat = 0.02 min-1 and Km = 5.0 mM for aniline in the presence of NADPH, 7-acetylflavin, and O at pH 7, whereas Fe coproporphyrin I showed only negligible activity under the same conditions.

IT **118475-37-9P**
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation and **condensation** with peptide amide)
RN 118475-37-9 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[N-[N2-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl]-L-α-glutamyl]-L-glutaminyl]-L-leucyl]-L-leucyl]-L-glutaminyl]-, 5,5'-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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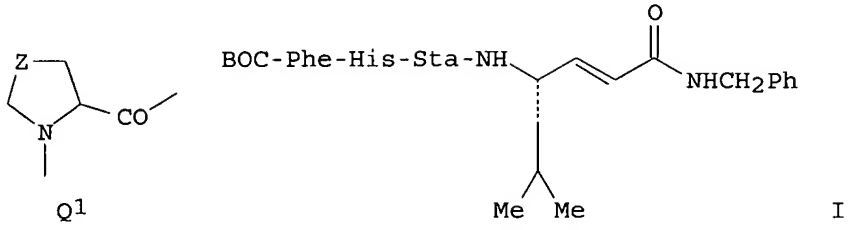
L17 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:6427 HCAPLUS
DOCUMENT NUMBER: 108:6427
TITLE: Preparation of peptide renin inhibitors as cardiovascular agents
INVENTOR(S): Boger, Joshua S.; Bock, Mark G.; Freidinger, Roger; Veber, Daniel F.; Patchett, Arthur A.; Greenlee, William J.; Parsons, William H.
PATENT ASSIGNEE(S): Merck and Co., Inc. , USA
SOURCE: Eur. Pat. Appl., 264 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 209897	A2	19870128	EP 1986-110125	19860723 <--
EP 209897	A3	19890816		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
CA 1290097	A1	19911001	CA 1986-514234	19860721 <--
DK 8603496	A	19870125	DK 1986-3496	19860723 <--
ES 2002469	A6	19880816	ES 1986-526	19860723 <--

JP 63030498 A2 19880209 JP 1986-172937 19860724 <--
PRIORITY APPLN. INFO.: US 1985-758625 A 19850724
GI



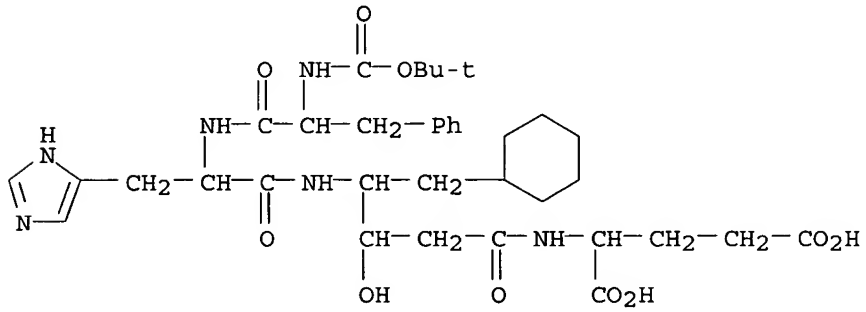
I

AB A-B-B-D-E-NHCH2R1CO-G-J [I; A = H, R2R21XCO; R2,R21 = H, alkyl, (substituted) aralkyl; X = O, OCH, CHO, CH, NHCH, SCH; B = null, Gly, Sar, HNCH(CH2R11)CO; R1,R11 = H, alkyl, hydroxyalkyl, (substituted) aryl; D = null, Q1; Z = CH, CH2CH2, S; E = null, HNCH[(CH2)mR5]CO; R3 = R5 = H, alkyl, (substituted) aryl, arylalkyl; G = HNCH[(CH2)qR6]QCHR4C:X1, HNCH[(CH2)qR6]CH(OH)CH[(CH2)qR61] C:X1; R4 = H, CHR3R9; R9 = H, alkyl, OH, cycloalkyl; R6 = alkyl, (substituted) cycloalkyl, aryl; R61 = H, cycloalkyl, (substituted) alkyl, aryl; Q = CONH, CSNH, CO2, COCH2, C(:CH2)CH2, HC:CH, P(:O)X2W, etc.; X2 = OH, alkoxy; W = bond, O, NH, CH2; J = Y (CH2)nR7 , Y[(CH2)rR8]R9, etc.; Y = NH, N(CH2)sR71, O; R7,R71 = H, (substituted) aryl; R8 = H, OH, amino; R81 = alkyl, cycloalkyl, (substituted) aryl; q, m = 1-4; n, r, s = 0-5] were prepared for treatment of hypertension, congestive heart failure, and hyperaldosteronism (no data). Peptidylbutenamide I (BOC = tert-butoxycarbonyl, Sta = 4-amino-3-hydroxy-6-methylheptanoic acid residue) was prepared by coupling BOC-Phe-His-Sta-NHNH2 with the corresponding aminobutenamide in the presence of isoamyl nitrite.

IT **111674-48-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; BIOL (Biological study); PREP (Preparation)
(preparation of, as cardiovascular agent)

RN 111674-48-7 HCAPLUS

CN L-Glutamic acid, N-[5-cyclohexyl-2,4,5-trideoxy-4-[[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl]-L-histidyl]amino]-L-threo-pentonoyl]-N-methyl- (9CI) (CA INDEX NAME)



L17 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:560841 HCAPLUS

DOCUMENT NUMBER: 103:160841
TITLE: Blood group antigens. Synthesis of TN glycopeptides representing the N-terminus of human glycophorin AN and AMc
AUTHOR(S): Ferrari, B.; Pavia, A. A.
CORPORATE SOURCE: Lab. Chim. Bioorg., Fac. Sci. d'Avignon, Avignon, 84000, Fr.
SOURCE: Tetrahedron (**1985**), 41(10), 1939-44
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: French
OTHER SOURCE(S): CASREACT 103:160841

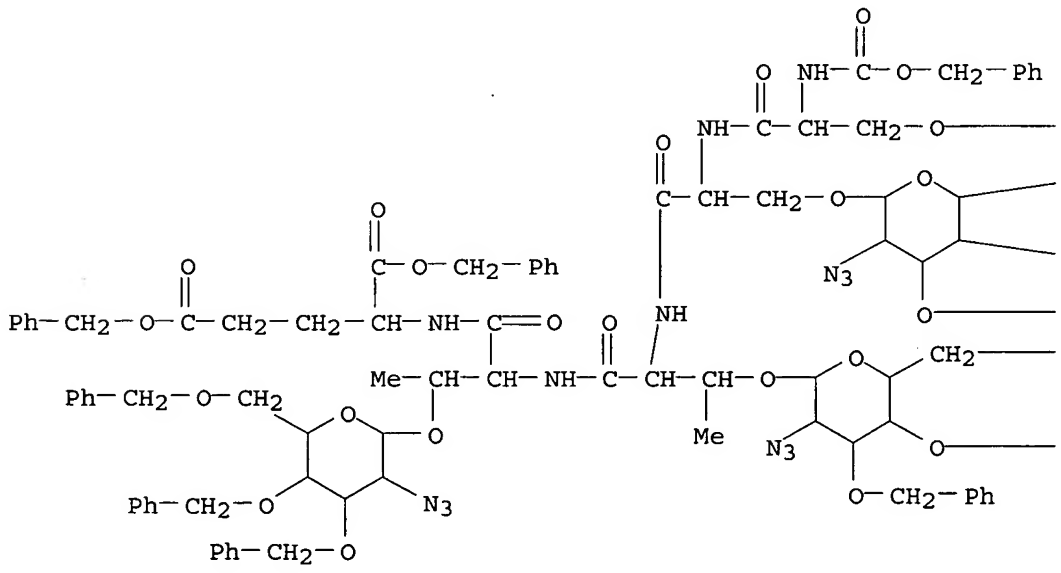
AB Title glycopeptides H-X-Ser(R)-Thr(R)-Thr(R)-Glu-OH (X = Leu or Ser; R = 2-acetamido-2-deoxy-α-D-galactopyranosyl residue) were prepared by stepwise couplings in solution Carbohydrate residues were introduced into the sequence as 2-azido-2-deoxy-α-D-galactopyranosyl-L-serine and L-threonine derivs. obtained from the reducing sugar and amino acid by the trifluoromethanesulfonic anhydride procedure. **Reduction** of the azido functions followed by acetylation and catalytic hydrogenolysis afforded the antigenic TN glycosylated pentapeptides.

IT **98619-51-3P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and borohydride **reduction** of)

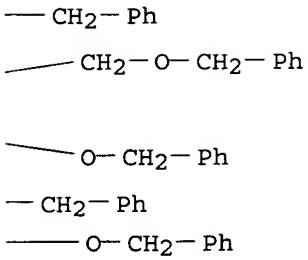
RN 98619-51-3 HCAPLUS

CN L-Glutamic acid, N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[N-[(phenylmethoxy)carbonyl]-O-(phenylmethyl)-L-seryl]-L-seryl]-L-threonyl]-L-threonyl]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

PAGE 1-A

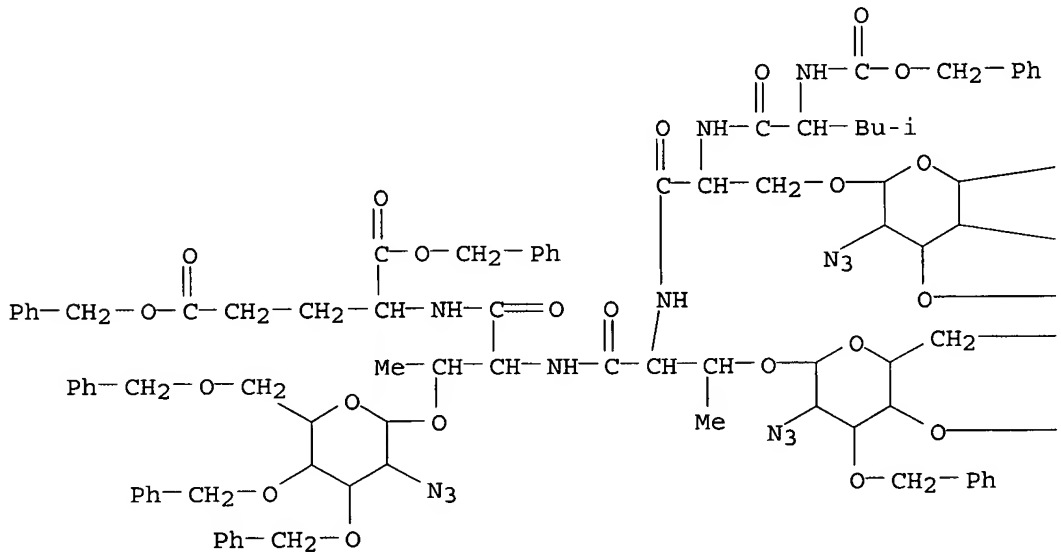


PAGE 1-B

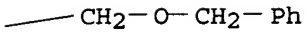


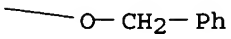
IT **98619-49-9P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydride **reduction** of)
RN 98619-49-9 HCAPLUS
CN L-Glutamic acid, N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[N-[(phenylmethoxy)carbonyl]-L-leucyl]-L-seryl]-L-threonyl]-L-threonyl]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

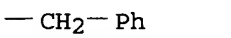
PAGE 1-A

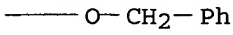


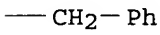
PAGE 1-B











IT **98619-50-2P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)
RN 98619-50-2 HCAPLUS
CN L-Glutamic acid, N-[O-[2-(acetylamino)-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[O-[2-(acetylamino)-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[O-[2-(acetylamino)-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[N-[(phenylmethoxy)carbonyl]-L-leucyl]-L-seryl]-L-threonyl]-L-threonyl]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

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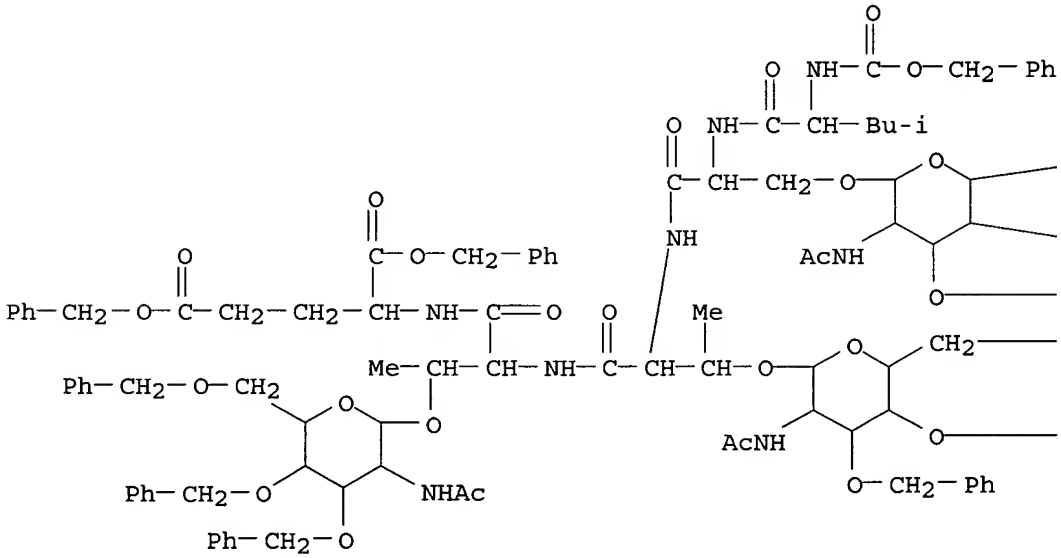

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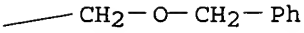

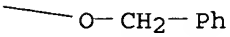

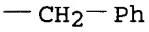

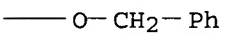

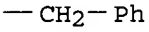

IT **98619-46-6P 98619-47-7P**
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation and partial deblocking of)
RN 98619-46-6 HCAPLUS
CN L-Glutamic acid, N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-threonyl]-L-threonyl]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

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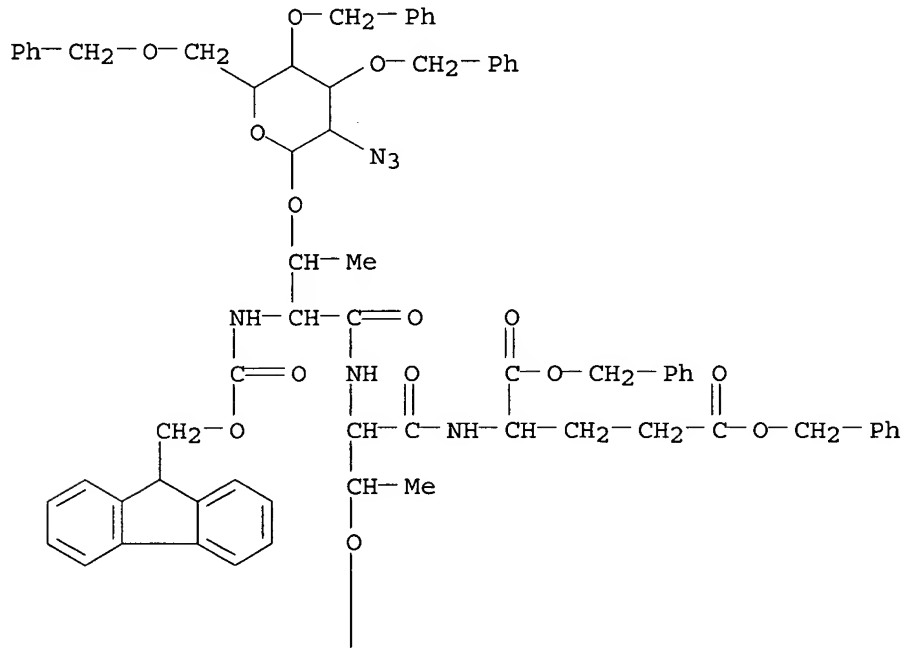

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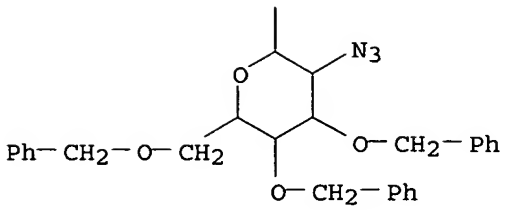

RN 98619-47-7 HCAPLUS
CN L-Glutamic acid, N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-seryl]-L-threonyl]-L-threonyl]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

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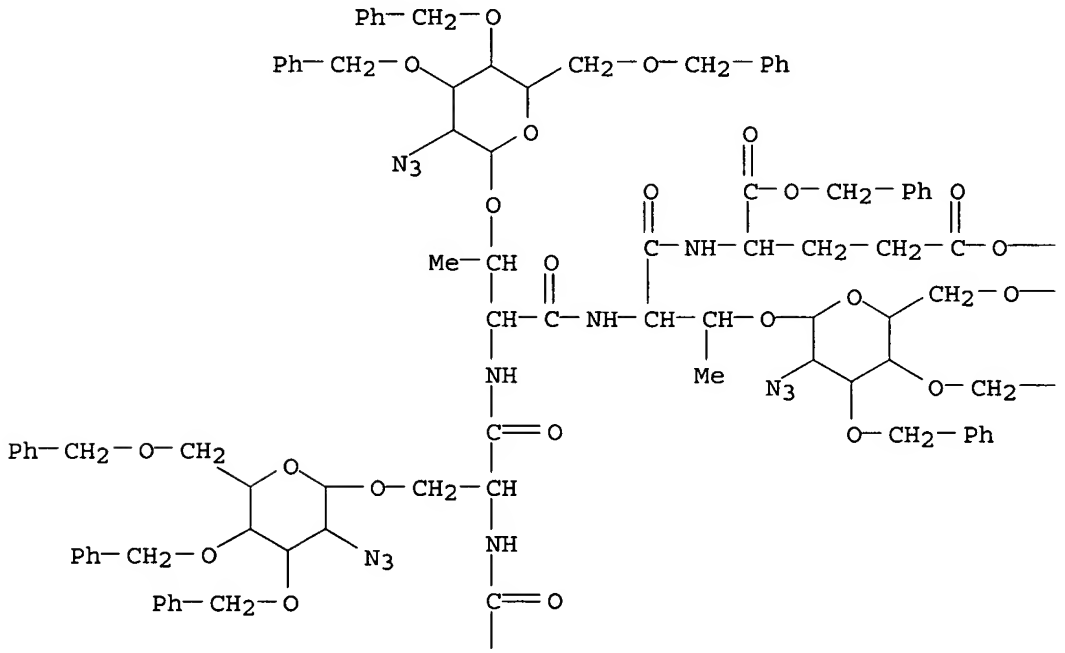

PAGE 1-B

—CH_2—Ph

—CH_2—Ph

—Ph

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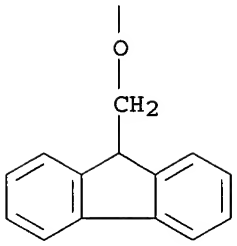

IT **98619-48-8P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of)
RN 98619-48-8 HCAPLUS
CN L-Glutamic acid, N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-L-seryl]-L-threonyl]-L-threonyl]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

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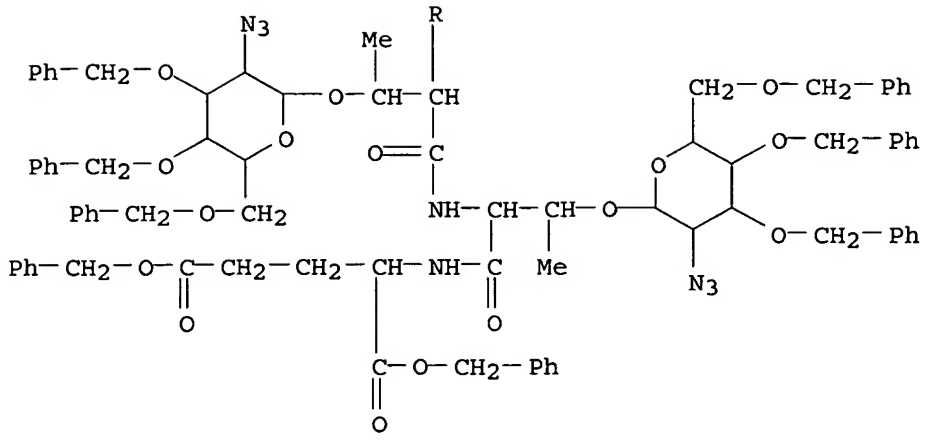

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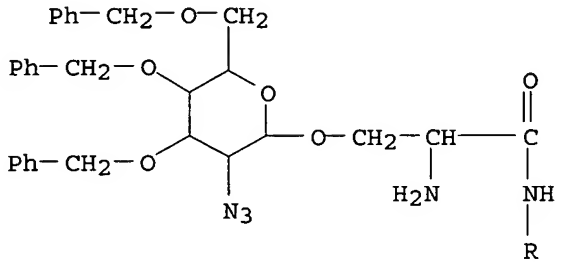

IT **98619-55-7P**
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation and peptide coupling with serine derivative)
RN 98619-55-7 HCAPLUS
CN L-Glutamic acid, N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[O-[2-azido-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-L-threonyl]-L-threonyl]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

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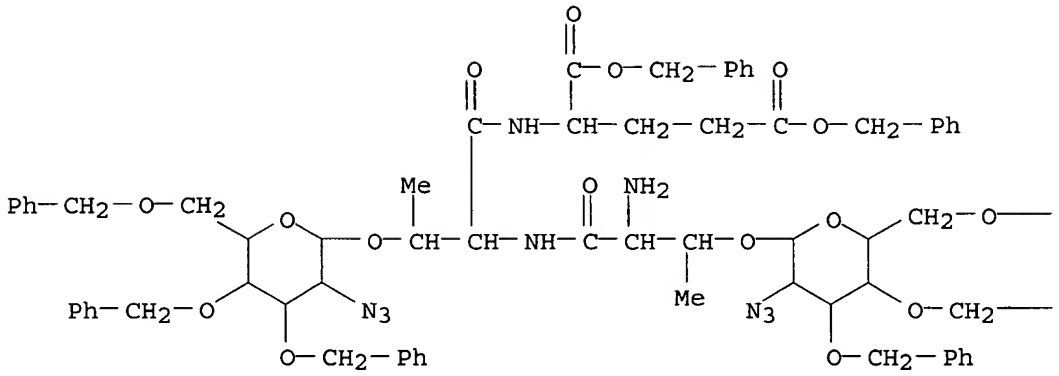

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— CH_2— Ph

— Ph

IT **98619-52-4P**
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation of)
RN 98619-52-4 HCAPLUS
CN L-Glutamic acid, N-[O-[2-(acetylamino)-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[O-[2-(acetylamino)-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[O-[2-(acetylamino)-2-deoxy-3,4,6-tris-O-(phenylmethyl)-α-D-galactopyranosyl]-N-[N-[(phenylmethoxy)carbonyl]-O-(phenylmethyl)-L-seryl]-L-seryl]-L-threonyl]-L-threonyl]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

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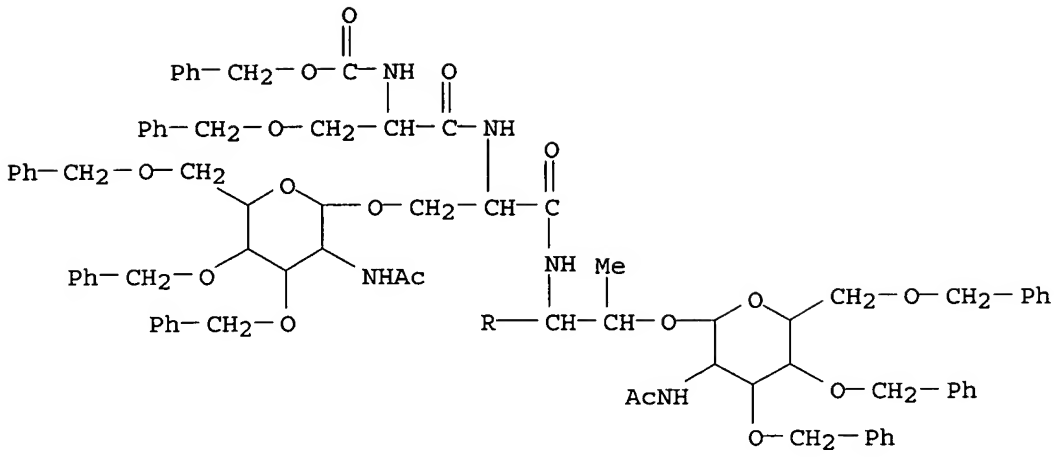

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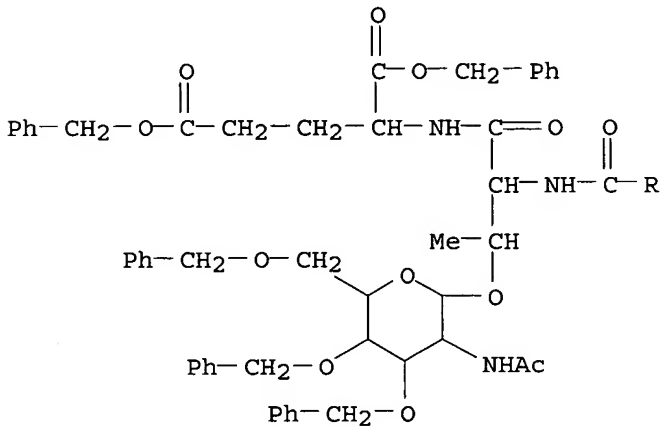
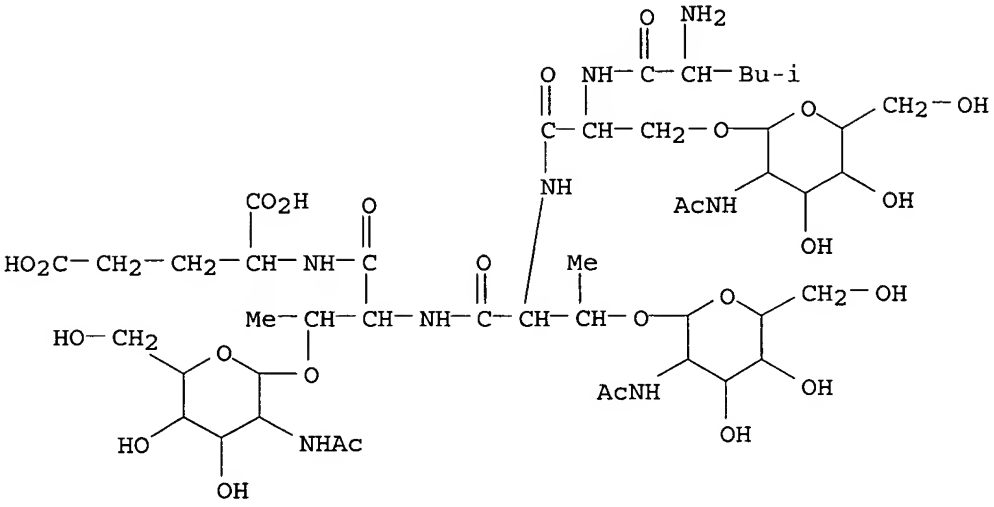
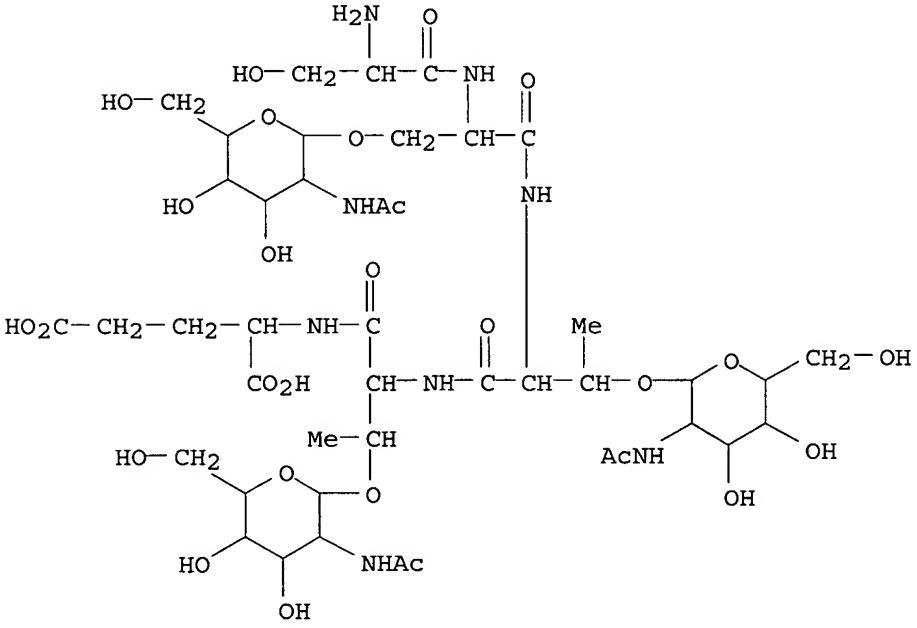


IT **98674-01-2P 98674-02-3P**
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation of, as antigenic amino-terminal portion of human glycophorin)
RN 98674-01-2 HCAPLUS
CN L-Glutamic acid, N-[O-[2-(acetylamino)-2-deoxy-α-D-galactopyranosyl]-N-[O-[2-(acetylamino)-2-deoxy-α-D-galactopyranosyl]-N-[O-[2-(acetylamino)-2-deoxy-α-D-galactopyranosyl]-N-L-leucyl-L-seryl]-L-threonyl]-L-threonyl]- (9CI) (CA INDEX NAME)



RN 98674-02-3 HCAPLUS
CN L-Glutamic acid, N-[O-[2-(acetylamino)-2-deoxy-α-D-galactopyranosyl]-N-[O-[2-(acetylamino)-2-deoxy-α-D-galactopyranosyl]-N-[O-[2-(acetylamino)-2-deoxy-α-D-galactopyranosyl]-N-L-seryl-L-seryl]-L-threonyl]-L-threonyl]- (9CI) (CA INDEX NAME)



L17 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:221199 HCAPLUS
DOCUMENT NUMBER: 102:221199
TITLE: Carboxyalkyl peptide derivatives
INVENTOR(S): McCullagh, Keith; Wadsworth, Harry; Hann, Michael
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: Eur. Pat. Appl., 111 pp.

CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 126974	A1	19841205	EP 1984-104614	19840425 <--
EP 126974	B1	19880615		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
AU 8427222	A1	19841122	AU 1984-27222	19840424 <--
AU 575048	B2	19880721		
ZA 8403056	A	19850626	ZA 1984-3056	19840425 <--
CA 1284850	A1	19910611	CA 1984-452746	19840425 <--
JP 59205350	A2	19841120	JP 1984-85091	19840426 <--
JP 06045635	B4	19940615		
JP 06316594	A2	19941115	JP 1993-256172	19931013 <--
JP 2725690	B2	19980311		
JP 08259593	A2	19961008	JP 1996-35137	19960222 <--
JP 2706646	B2	19980128		

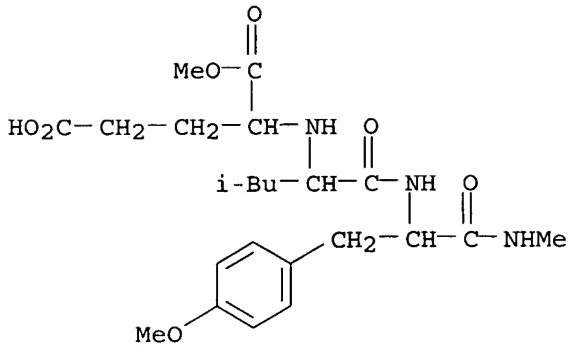
PRIORITY APPLN. INFO.: GB 1983-11286 A 19830426

AB Carboxylalkyl peptides A1A2-X-(CH2)nCH(COR1)NHCR2R3COA3 [n = 1-4; R1 = H, alkoxy, aralkoxy, NHOH; R2 = H, alkyl; R3 = H, (un)substituted alkyl, (un)substituted aralkyl, heteroaralkyl; X = NR4 (R4 = H, alkyl), A1 = H, alkyl, aralkyl, acyl, aroyl, aralkylacyl, alkoxycarbonyl, aralkoxycarbonyl, (un)substituted aryl, α-aminoacyl, A2 = α-amino acid residue, A1A2 = H, alkyl, aralkyl, heteroalkyl, alkylsulfonyl, acyl, etc.; X = bond, A1A2 = H, alkyl, aryl, alkoxy, substituted aryl, (un)substituted aralkoxy; A3 = NH2, alkylamino, dialkylamino, NHOH, aralkylamino, or amino acid residue] were prepared as collagenase inhibitors and they can be used for the treatment of rheumatoid arthritis. Thus, H-L-Leu-OCH2Ph tosylate underwent **reductive** alkylation with Me pyruvate in the presence of NaBH3CN to give (R)-CH3CH(CO2Me)-L-Leu-OR5 (I, R5 = CH2Ph) (II) and its S-diastereoisomer, which were separated by column chromatog. on SiO2. II was debenzylated by hydrogenolysis over Pd/C to give 82% I (R5 = H) (III). Boc-L-Tyr(CH2Ph)-NHMe (Boc = Me3CO2C) was Boc-deblocked by CF3CO2H/CH2Cl2 and then coupled with III by DCC/1-hydroxybenzotriazole give 68% (R)-CH3CH(CO2R6)-L-Leu-L-Tyr(CH2Ph)-NHMe (IV, R6 = Me), which was saponified to give IV (R6 = H) (V). V inhibited human rheumatoid synovial collagenase with an IC50 = 1.7 μM.

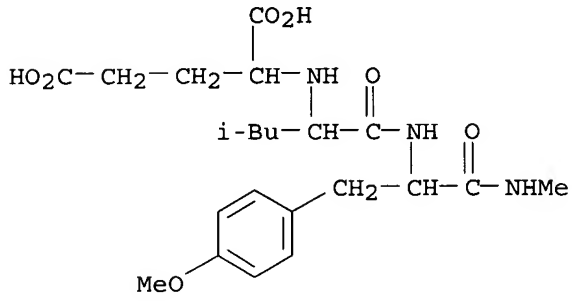
IT **96135-05-6P 96135-06-7P**
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation of)

RN 96135-05-6 HCAPLUS

CN L-Tyrosinamide, N-[3-carboxy-1-(methoxycarbonyl)propyl]-L-leucyl-N,O-dimethyl-, (R)- (9CI) (CA INDEX NAME)



RN 96135-06-7 HCAPLUS
CN L-Tyrosinamide, N-(1,3-dicarboxypropyl)-L-leucyl-N,O-dimethyl-, (R)- (9CI) (CA INDEX NAME)



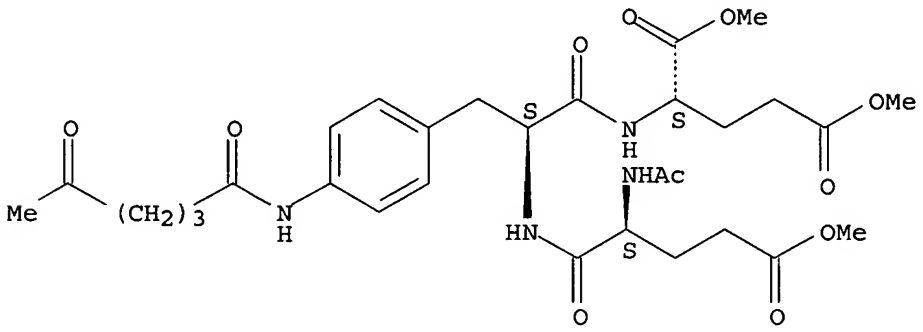
L17 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:175255 HCAPLUS
DOCUMENT NUMBER: 100:175255
TITLE: Conjugates of catecholamines. III. Synthesis and characterization of monodisperse oligopeptides conjugates related to isoproterenol
AUTHOR(S): Jacobson, K. A.; Verlander, M. S.; Rosenkranz, R. P.; Melmon, K. L.; Goodman, Murray
CORPORATE SOURCE: Dep. Chem., Univ. California, San Diego, La Jolla, CA, USA
SOURCE: International Journal of Peptide & Protein Research (**1983**), 22(3), 284-304
CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of monodisperse oligopeptide conjugates related to the catecholamine isoproterenol was prepared The peptide carrier mols. used were synthesized by stepwise and fragment **condensation** techniques and ranged in size from a single, blocked amino acid derivative to isometric pentapeptides. The amino acid compns. and sequences of the carriers were chosen so as to provide specific information concerning the effects of mol. weight, hydrophilic/hydrophobic balance, charge, etc., on the biol. activity of the final conjugates. The common point of attachment for the drug in all carriers was a p-aminophenylalanine residue. The peptide-catecholamine conjugates were prepared via the attachment of carboxyl-containing catecholamine congeners to the peptide carriers by

techniques described previously. The conjugates were purified rigorously by chromatog. techniques and characterized by high-field NMR spectroscopy.

IT **89545-99-3P 89546-04-3P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation of, with methylamine)

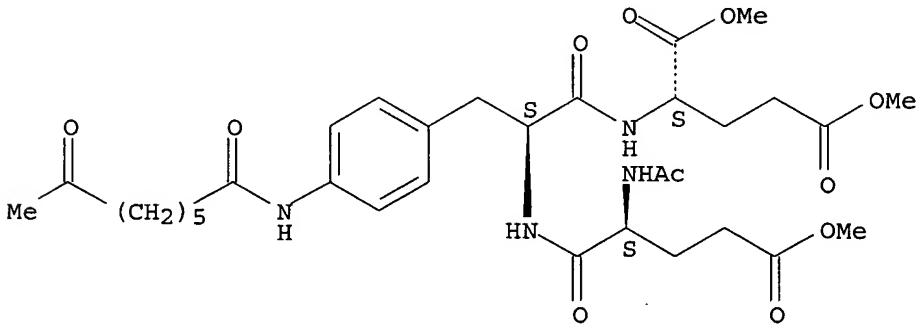
RN 89545-99-3 HCAPLUS
CN L-Glutamic acid, N-[N-(N-acetyl-L-α-glutamyl)-4-[(1,5-dioxohexyl)amino]-L-phenylalanyl]-, trimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 89546-04-3 HCAPLUS
CN L-Glutamic acid, N-[N-(N-acetyl-L-α-glutamyl)-4-[(1,7-dioxooctyl)amino]-L-phenylalanyl]-, trimethyl ester (9CI) (CA INDEX NAME)

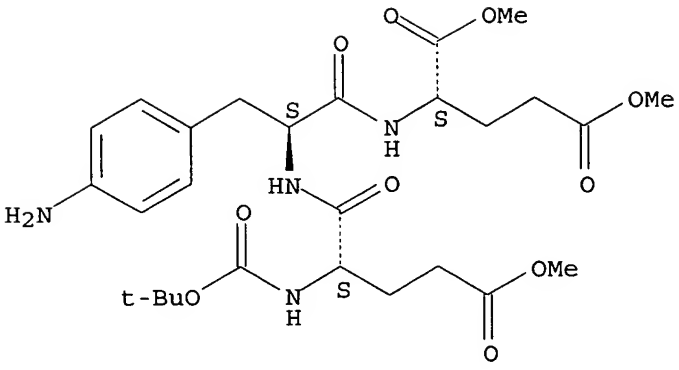
Absolute stereochemistry.



IT **89545-97-1P**
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation and **condensation** of, with oxo alkanoic acids)

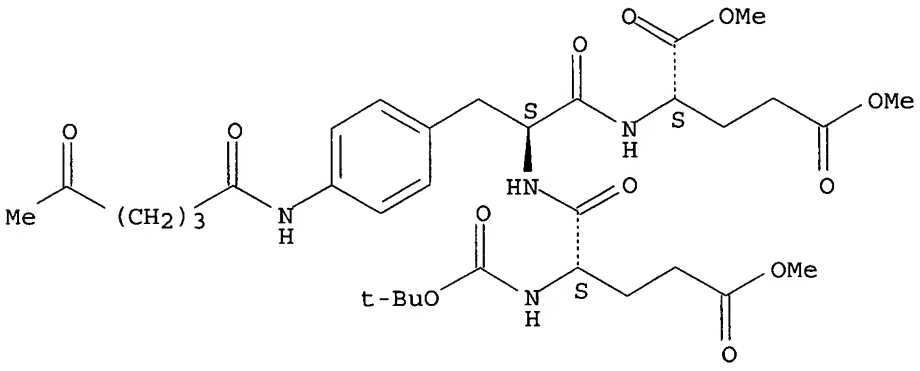
RN 89545-97-1 HCAPLUS
CN L-Glutamic acid, N-[4-amino-N-[N-[(1,1-dimethylethoxy)carbonyl]-L-α-glutamyl]-L-phenylalanyl]-, trimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



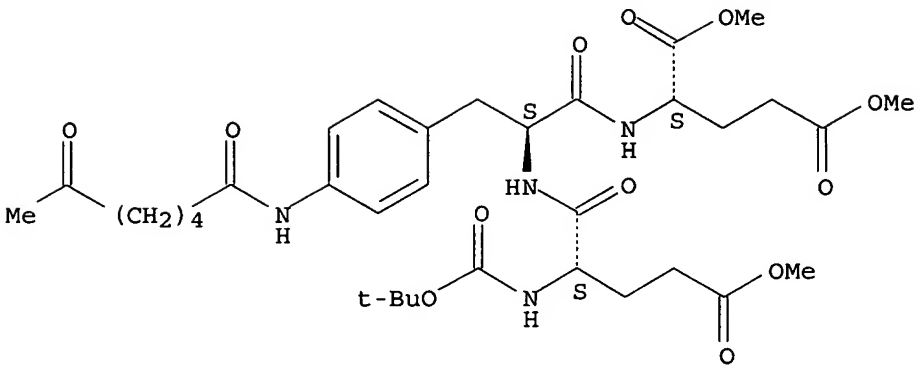
IT **89545-98-2P 89546-01-0P 89546-03-2P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection-acetylation of)
RN 89545-98-2 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-α-glutamyl]-4-[(1,5-dioxohexyl)amino]-L-phenylalanyl]-, trimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



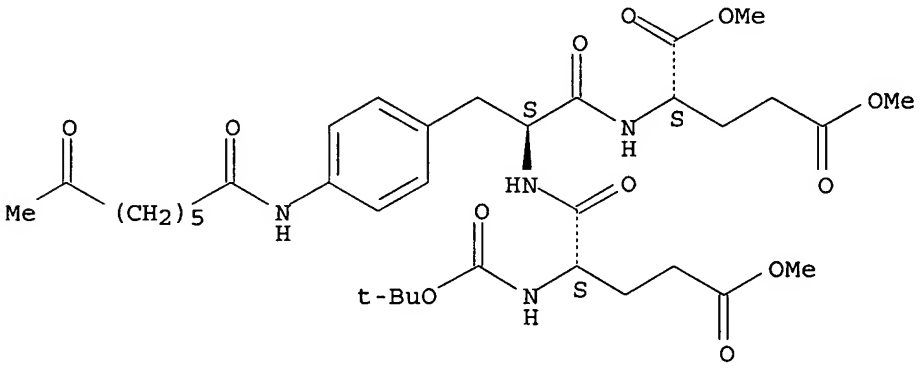
RN 89546-01-0 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-α-glutamyl]-4-[(1,6-dioxoheptyl)amino]-L-phenylalanyl]-, trimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



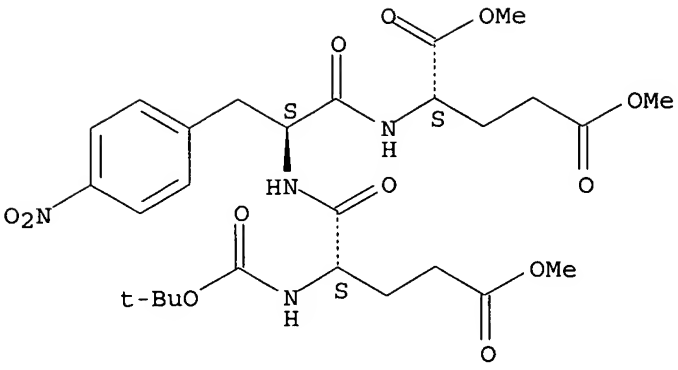
RN 89546-03-2 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-α-glutamyl]-4-[(1,7-dioxooctyl)amino]-L-phenylalanyl]-, trimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



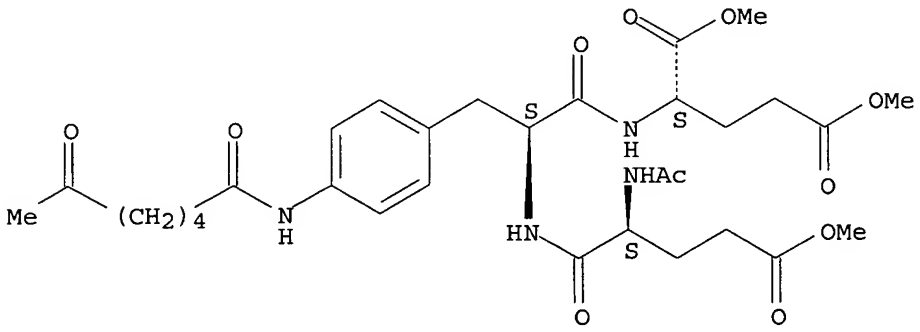
IT **89545-96-0P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of)
RN 89545-96-0 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-α-glutamyl]-4-nitro-L-phenylalanyl]-, trimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **89546-02-1P**
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation and **reductive** amination with epinephrine)
RN 89546-02-1 HCAPLUS
CN L-Glutamic acid, N-[N-(N-acetyl-L-α-glutamyl)-4-[(1,6-dioxoheptyl)amino]-L-phenylalanyl]-, trimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:558822 HCAPLUS
DOCUMENT NUMBER: 99:158822
TITLE: The synthesis of precursors of labeled neuropeptides
AUTHOR(S): Van Nispen, J. W.; Bijl, W. A. A. J.; Hendrix, A. M. M.; Greven, H. M.
CORPORATE SOURCE: Sci. Dev. Group, Organon Int. B.V., Oss, 5340 BH, Neth.
SOURCE: Recueil: Journal of the Royal Netherlands Chemical Society (**1983**), 102(5), 276-83
CODEN: RJRSDK; ISSN: 0165-0513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Modified amino acids which can serve as precursors in the synthesis of tritium-labeled peptides were prepared and incorporated into biol. active peptides. Thus, p-iodophenylalanine was incorporated at position 4 of H-Met(O2)-Glu-His-Phe-D-Lys-Phe-OH (I) and in des-Tyr1-γ-endorphin. As a second labeling site, the precursor of L-leucine, L-methallylglycine, was incorporated in both des-Tyr1-γ-endorphin and the shorter

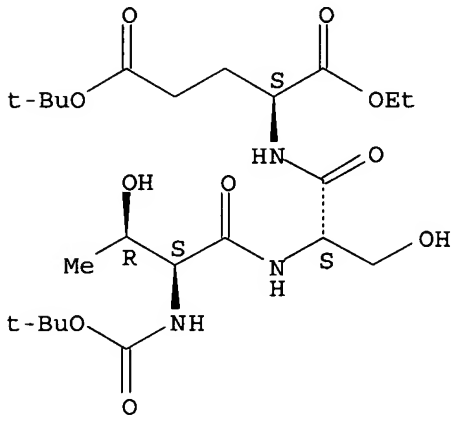
des-enkephalin-γ-endorphin (II). The lysine residues in I and II in were replaced by 2,6-diamino-4-hexynoic acid. The precursor peptides were synthesized via the fragment **condensation** approach. With the exception of the methallylglycine-containing des-Tyr1-γ-endorphin, in which partial desulfurization of the methionine residue could not be prevented, these peptides could be converted by means of catalytic **reduction** into their resp. parent compds.

IT **87325-74-4P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrazinolysis of)

RN 87325-74-4 HCAPLUS

CN L-Glutamic acid, N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-threonyl]-L-seryl]-, 5-(1,1-dimethylethyl) 1-ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1982:598545 HCAPLUS

DOCUMENT NUMBER: 97:198545

TITLE: A new protecting group combination for solid phase synthesis of protected peptides

AUTHOR(S): Sheppard, Robert C.; Williams, Brian J.

CORPORATE SOURCE: Lab. Mol. Biol., MRC Cent., Cambridge, CB2 2QH, UK

SOURCE: Journal of the Chemical Society, Chemical Communications (**1982**), (11), 587-9
CODEN: JCCCAT; ISSN: 0022-4936

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Protected peptides suitable for fragment **condensation** strategies were prepared by a solid-phase method using Nα-fluorenylmethoxycarbonyl (Fmoc) amino acids in combination with tert-Bu-based side-chain protective groups and 1,2-(HOCH2)(MeO)C6H3OCH2CO2H-4 to link the peptide to poly(dimethylacrylamide) resins. Thus, gastrin fragments Fmoc-Glu(OCMe3)-Ala-Tyr(CMe3)-Gly-OH and Fmoc-Leu-Glu(OCMe3)-OH were prepared by theabove solid-phase method.

IT **83619-41-4P**
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation of, by solid-phase method)

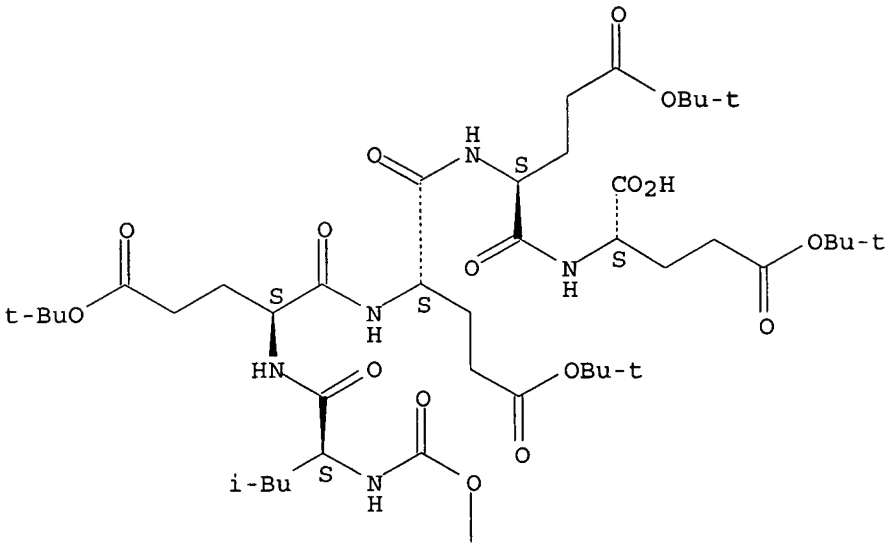
RN 83619-41-4 HCAPLUS

CN L-Glutamic acid, N-[N-[N-[N-[N-[(9H-fluoren-9-yloxy)carbonyl]-L-leucyl]-L-α-glutamyl]-L-α-glutamyl]-L-α-glutamyl]-,

5,5',5'',5'''-tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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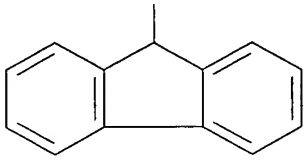


L17 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:611834 HCAPLUS
DOCUMENT NUMBER: 91:211834
TITLE: Basic pancreatic trypsin-inhibitor (BPTI) derivatives
INVENTOR(S): Schnabel, Eugen; Reinhardt, Gerd; Schlumberger, Horst Dieter; Opitz, Hans Georg; Truscheit, Ernst; Tschesche, Harald
PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 88 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

DE 2748295	A1	19790503	DE 1977-2748295	19771027 <--
EP 1774	A1	19790516	EP 1978-101147	19781014 <--
R: BE, CH, DE, FR, GB, NL, SE				
JP 54073702	A2	19790613	JP 1978-130614	19781025 <--
DK 7804771	A	19790428	DK 1978-4771	19781026 <--
ES 474559	A1	19791016	ES 1978-474559	19781026 <--

PRIORITY APPLN. INFO.: DE 1977-2748295 19771027

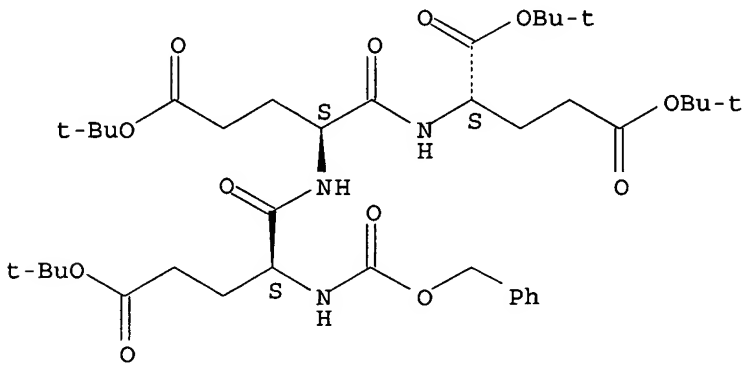
AB Modified BPTI derivs., useful as proteinase inhibitors and inflammation inhibitors, were prepared by the **condensation** of BPTI or its derivs. containing free carboxy groups with nucleophilic amino compds. (e.g., amino acids or peptides) by carbodiimides in aqueous solution followed by deamination and/or azo coupling with diazonium compds. Thus, BPTI was coupled with N-methyl-L-threoninol in H2O by Me2N(CH2)3N:C:NEt for 6 h at 22° to give the corresponding BPTI derivative (I). I was deaminated by NaNO2/HOAc at 4° to give the deamino derivative, and coupled with 3,5-Cl2C6H3N2+ to give an orange-colored azo derivative Prepns. of a large number of modified BPTI derivs. (.apprx.80 examples) are given. Data are given on the inhibition of several proteinases (e.g., chymotrypsin, trypsin) by .apprx.27 modified BPTI derivs. Antiinflammatory data in rats are also given.

IT **26308-93-0P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)

RN 26308-93-0 HCAPLUS

CN L-Glutamic acid, N-[N-[N-[(phenylmethoxy)carbonyl]-L-α-glutamyl]-L-α-glutamyl]-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

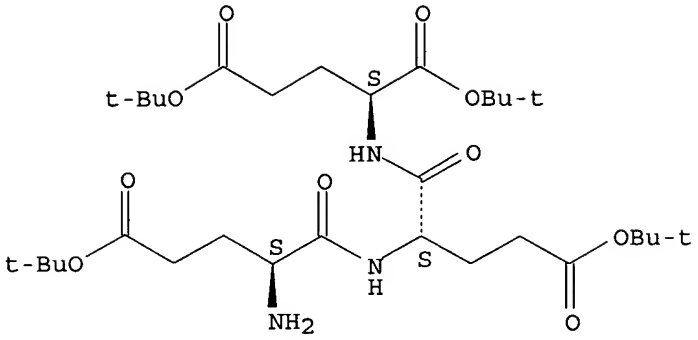


IT **69984-06-1P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with basic pancreatic trypsin inhibitor)

RN 69984-06-1 HCAPLUS

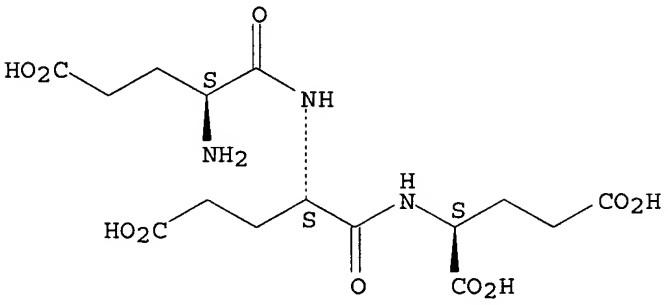
CN L-Glutamic acid, N-(N-L-α-glutamyl-L-α-glutamyl)-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **23684-48-2DP**, basic pancreatic trypsin inhibitor derivative
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation of)
RN 23684-48-2 HCAPLUS
CN L-Glutamic acid, L-α-glutamyl-L-α-glutamyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:439878 HCAPLUS
DOCUMENT NUMBER: 91:39878
TITLE: Polypeptides
INVENTOR(S): Fujino, Masahiko; Shinagawa, Susumu
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 24 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 54009267	A2	19790124	JP 1977-74756	19770622 <--
JP 61026559	B4	19860620		

PRIORITY APPLN. INFO.: JP 1977-74756 A 19770622
AB Motilin analogs H-Phe-Val-Pro-Ile-Phe-Thr-Tyr-X-Glu-Leu-X1-Arg-X2-Glu-Glu-X3-OH [I; X = Gly, D-amino acid residue; X1 = Glu, Gln; X2 = Met, Met(O), Leu; X3 = bond, Lys-Glu-Arg-Asn-Lys-Gly-Gln] were prepared Thus, BOC-Glu(OCH2Ph)-Leu-Glu-Arg(MBS)-Met(O)-Glu-Glu(OCH2Ph)-OH (II; BOC =

Me3CO2C, MBS = p-MeOC6H4SO2) was BOC-deblocked and coupled to Z-Phe-Val-Pro-Ile-Phe-Thr-Tyr-Gly-OH (III, Z = PhCH2O2C) by dicyclohexylcarbodiimide/N-hydroxy-5-norbornene-2,3-dicarboximide to give Z-Phe-Val-Pro-Ile-Phe-Thr-Tyr-Gly-Glu(OCH2Ph)-Leu-Gln-Arg(MBS)-Met(O)-Gln-Glu(OCH2Ph)-OH, which was deblocked by MeSO3H/anisole to give I [X = Gly, X1 = Gln, X2 = Met(O), X3 = bond]. The sulfoxide was cleaved from the latter to give the corresponding I (X2 = Met). II and III were prepared by stepwise peptide couplings in solution

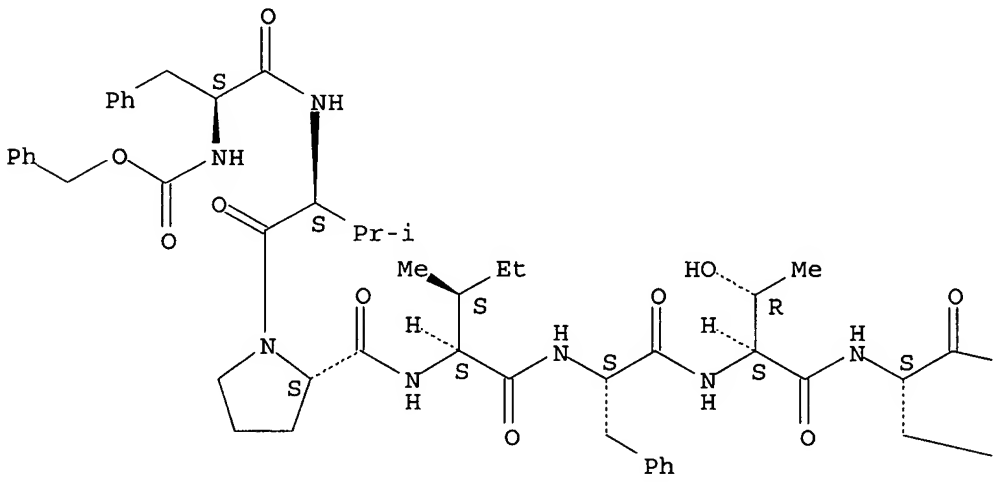
IT **70645-86-2P 70646-10-5P 70646-13-8P**
70646-15-0P 70646-19-4P 70646-22-9P
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and deblocking of)

RN 70645-86-2 HCAPLUS

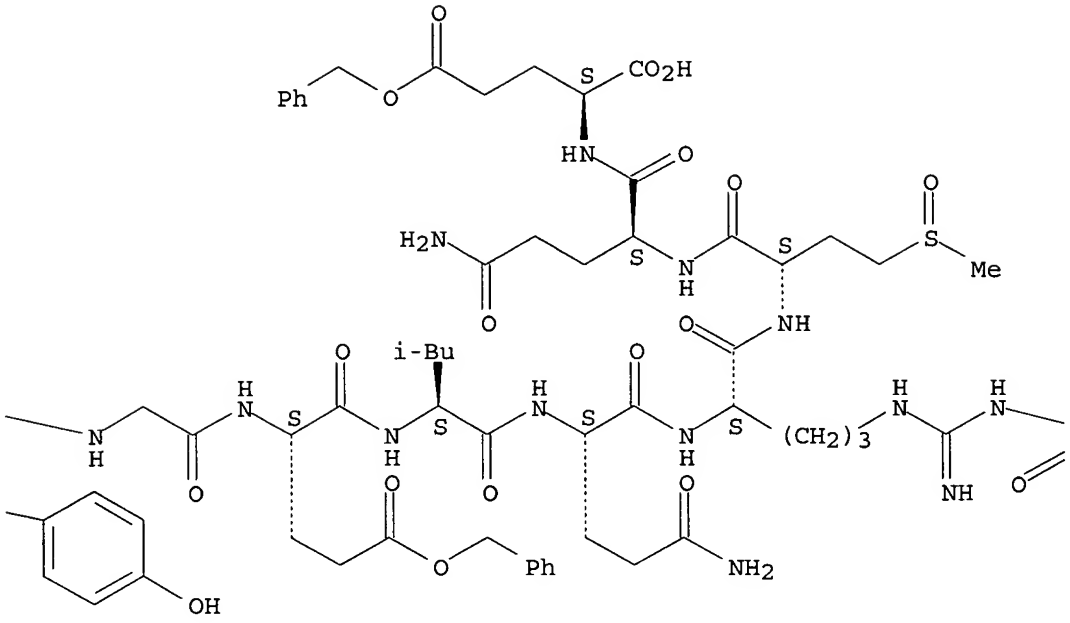
CN Motilin (swine), N-[(phenylmethoxy)carbonyl]-12-[N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithine]-13-[4-(methylsulfinyl)-L-2-aminobutanoic acid]-16-de-L-lysine-17-de-L-glutamic acid-18-de-L-arginine-19-de-L-asparagine-20-de-L-lysine-21-deglycine-22-de-L-glutamine-, 9,155-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

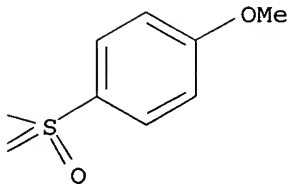
PAGE 1-A



PAGE 1-B



PAGE 1-C

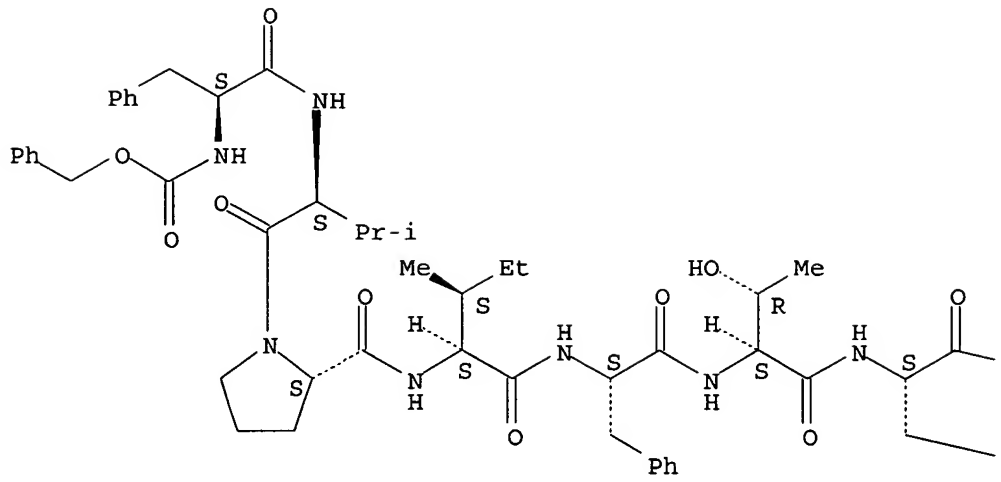


RN 70646-10-5 HCAPLUS

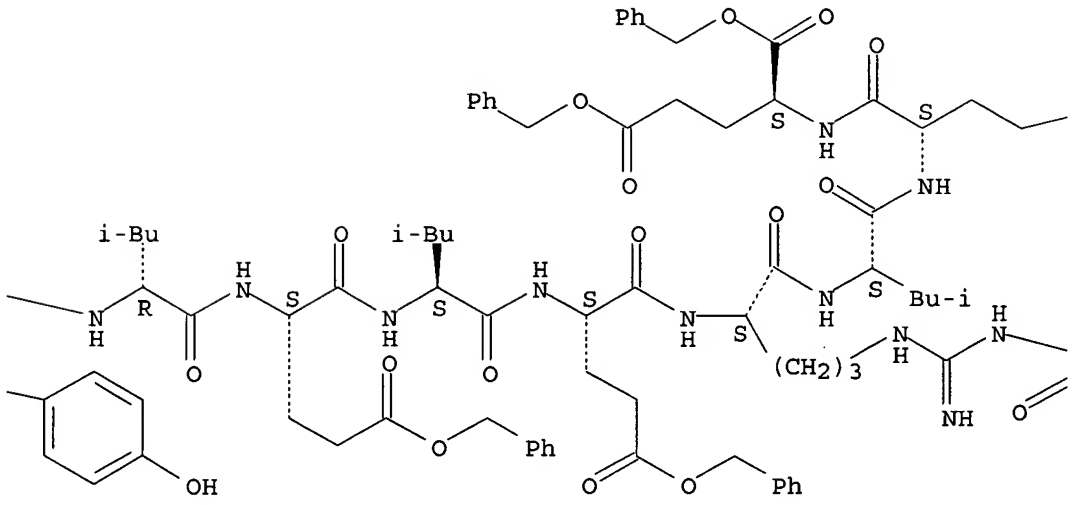
CN L-Glutamic acid, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-L-valyl-L-prolyl-L-isoleucyl-L-phenylalanyl-L-threonyl-L-tyrosyl-D-leucyl-L-α-glutamyl-L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-L-leucyl-L-glutaminyl-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

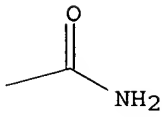
PAGE 1-A

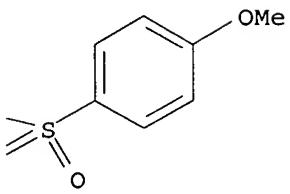


PAGE 1-B



PAGE 1-C

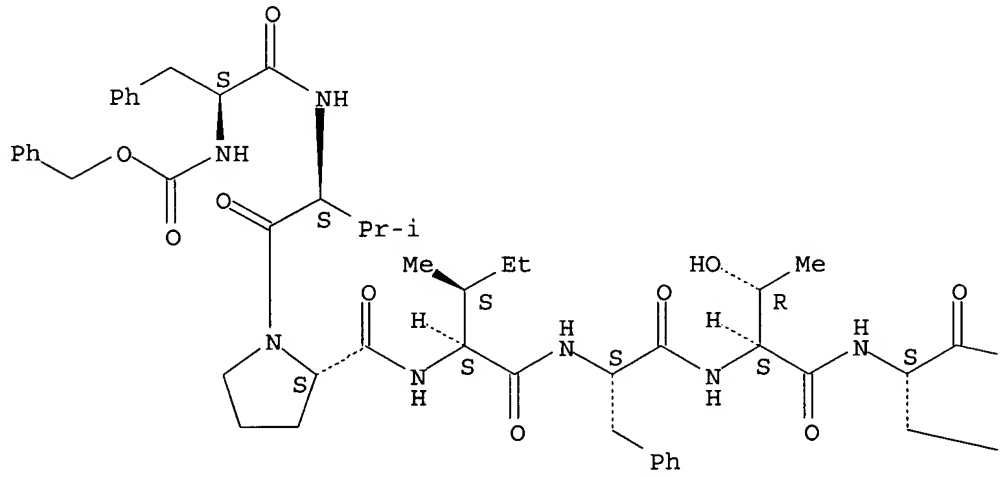




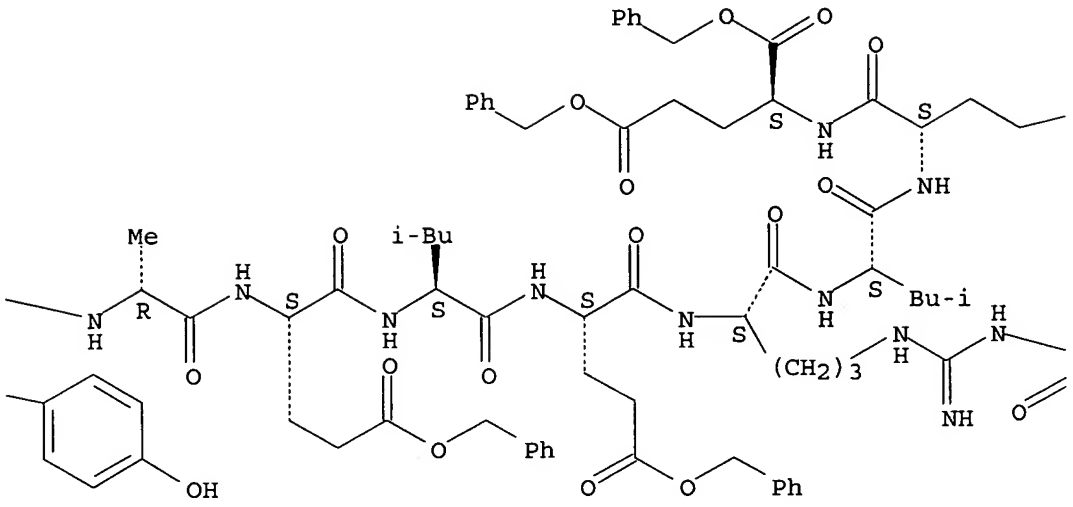
RN 70646-13-8 HCAPLUS
CN L-Glutamic acid, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-L-valyl-L-prolyl-L-isoleucyl-L-phenylalanyl-L-threonyl-L-tyrosyl-D-alanyl-L-α-glutamyl-L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-L-leucyl-L-glutaminyl-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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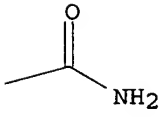
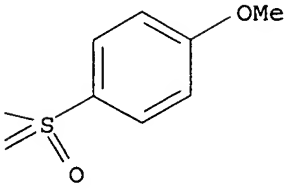


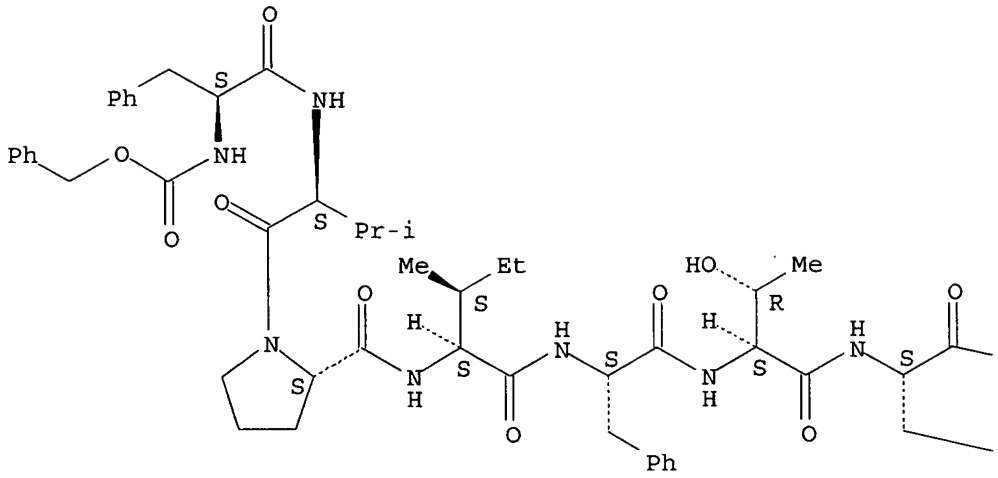


RN 70646-15-0 HCAPLUS

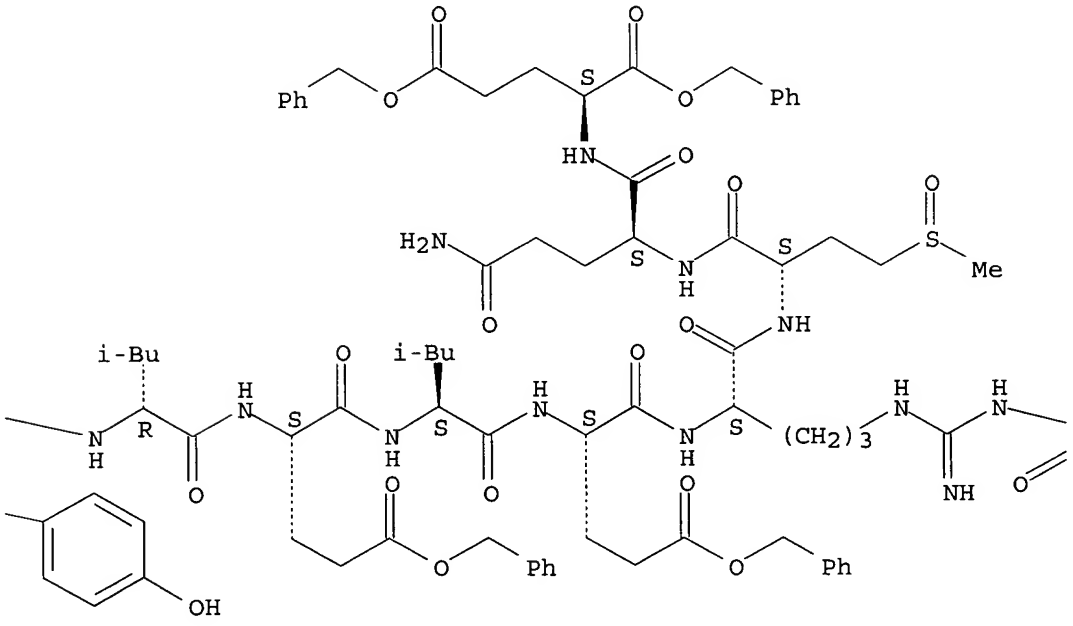
CN L-Glutamic acid, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-L-valyl-L-prolyl-L-isoleucyl-L-phenylalanyl-L-threonyl-L-tyrosyl-D-leucyl-L-α-glutamyl-L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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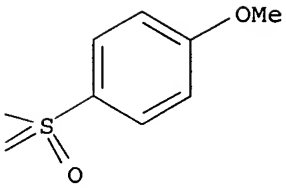
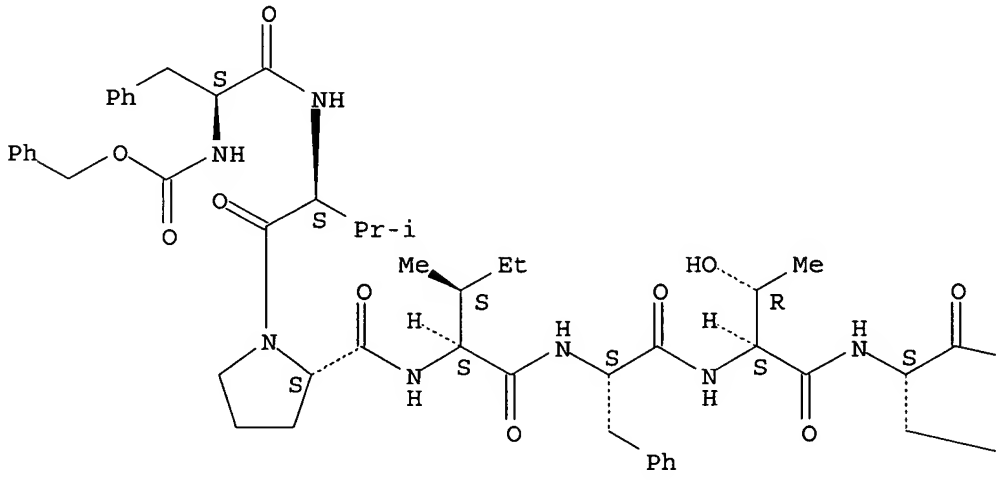


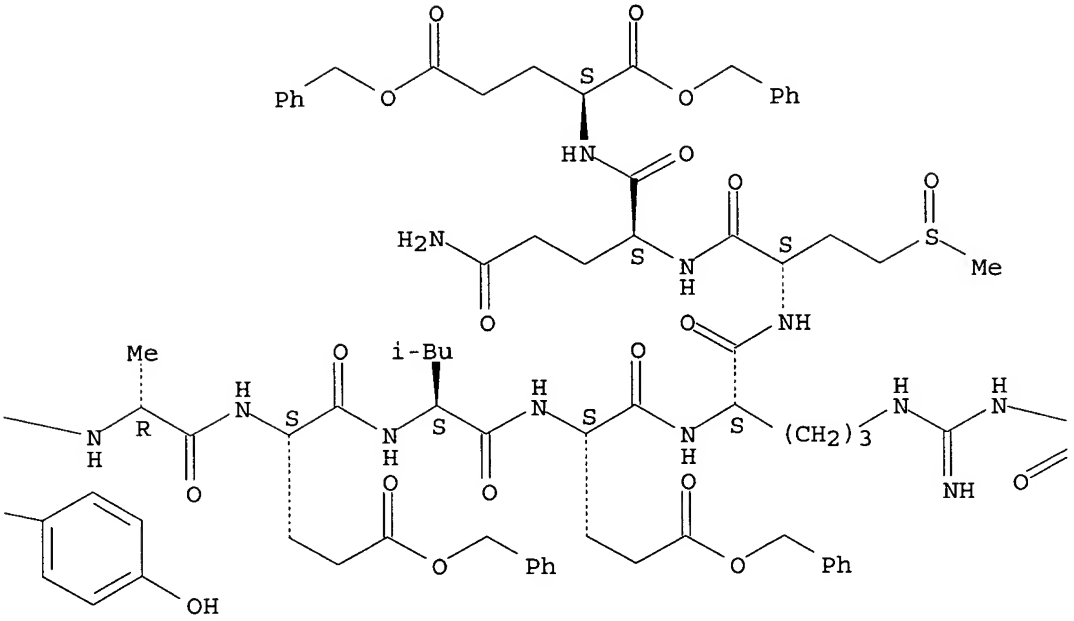
RN 70646-19-4 HCAPLUS
CN L-Glutamic acid, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-L-valyl-L-prolyl-L-isoleucyl-L-phenylalanyl-L-threonyl-L-tyrosyl-D-alanyl-L-α-glutamyl-L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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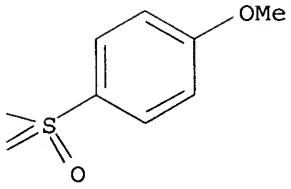
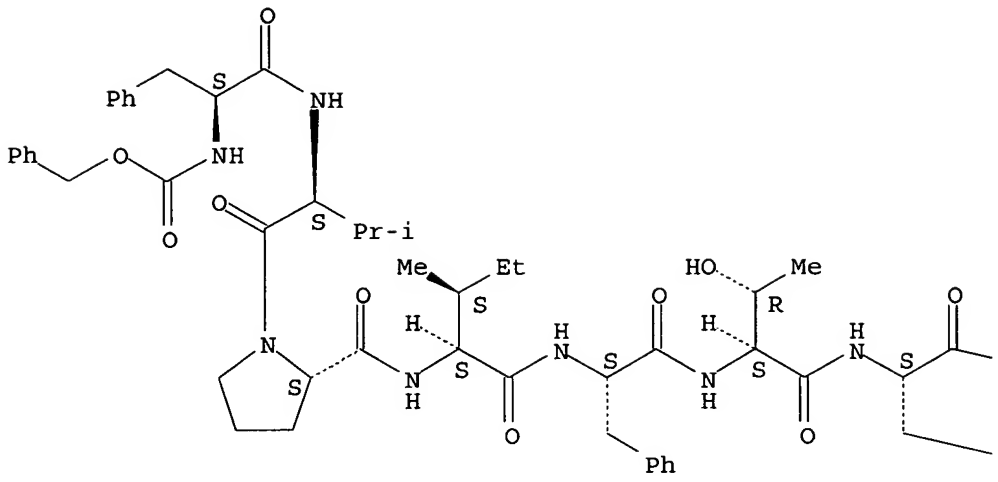


RN 70646-22-9 HCAPLUS

CN L-Glutamic acid, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-L-valyl-L-prolyl-L-isoleucyl-L-phenylalanyl-L-threonyl-L-tyrosylglycyl-L-α-glutamyl-L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-L-leucyl-L-glutaminyl-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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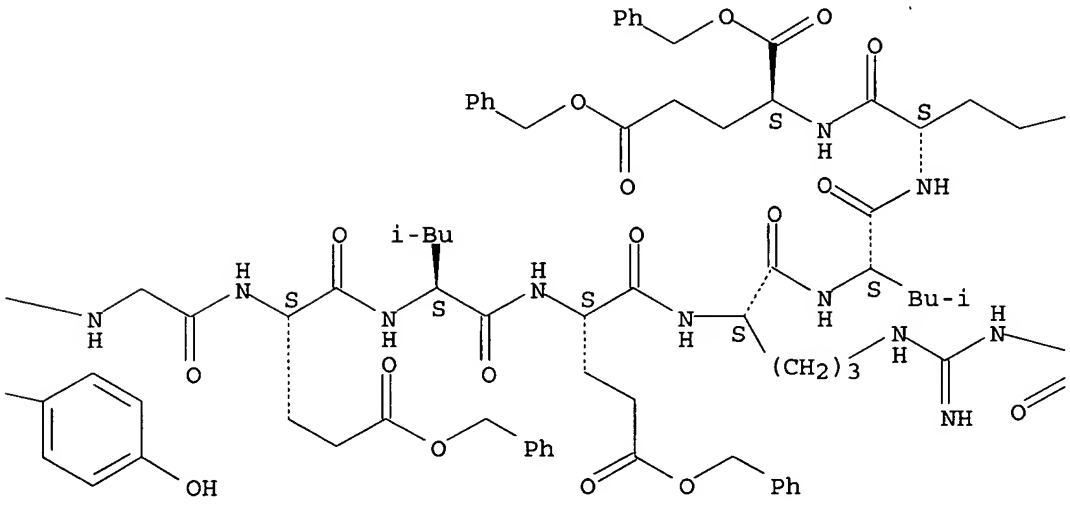
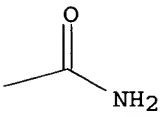
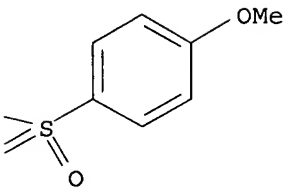




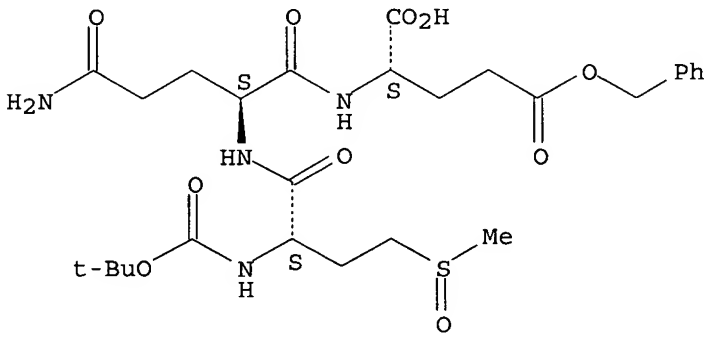


IT **66450-10-0P 66450-13-3P 66450-16-6P**
66450-18-8P 66450-21-3P 70645-89-5P
70645-91-9P 70645-99-7P 70646-00-3P
70646-02-5P 70646-04-7P 70646-06-9P
70646-08-1P 70655-63-9P 70655-65-1P
70655-67-3P 70655-69-5P 70655-71-9P
70673-08-4P
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation and partial deblocking of)

RN 66450-10-0 HCAPLUS

CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, 35-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

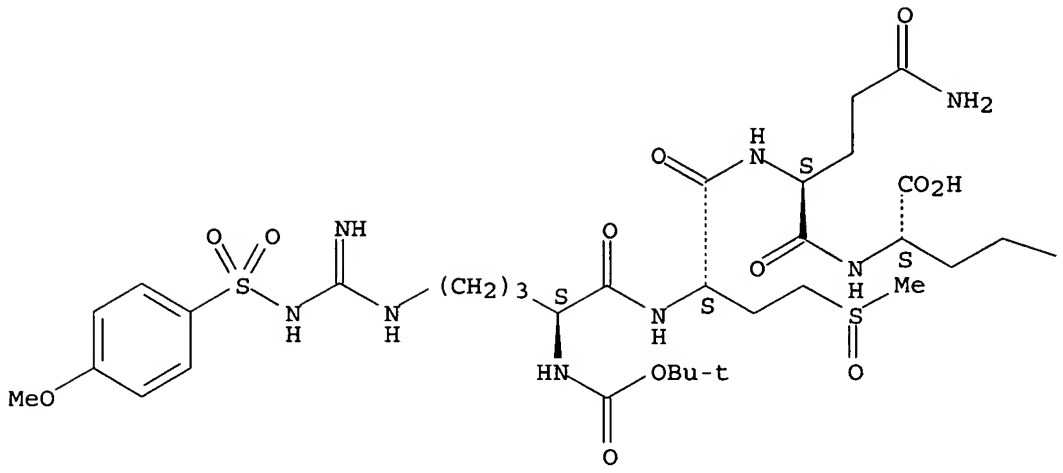


RN 66450-13-3 HCAPLUS

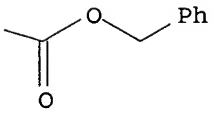
CN L-Glutamic acid, N2-[(1,1-dimethylethoxy)carbonyl]-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, 45-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

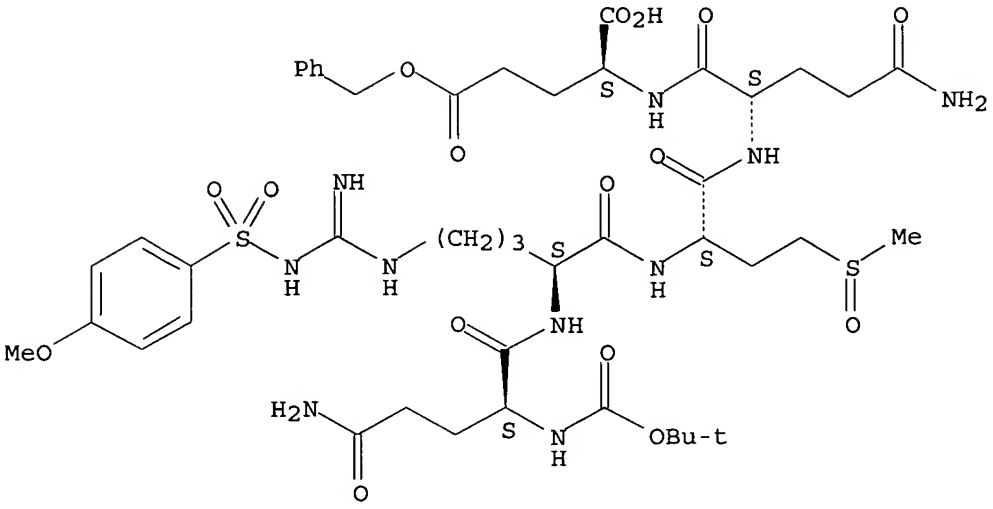


PAGE 1-B



RN 66450-16-6 HCAPLUS
CN L-Glutamic acid, N2-[(1,1-dimethylethoxy)carbonyl]-L-glutaminyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, 55-(phenylmethyl) ester (9CI) (CA INDEX NAME)

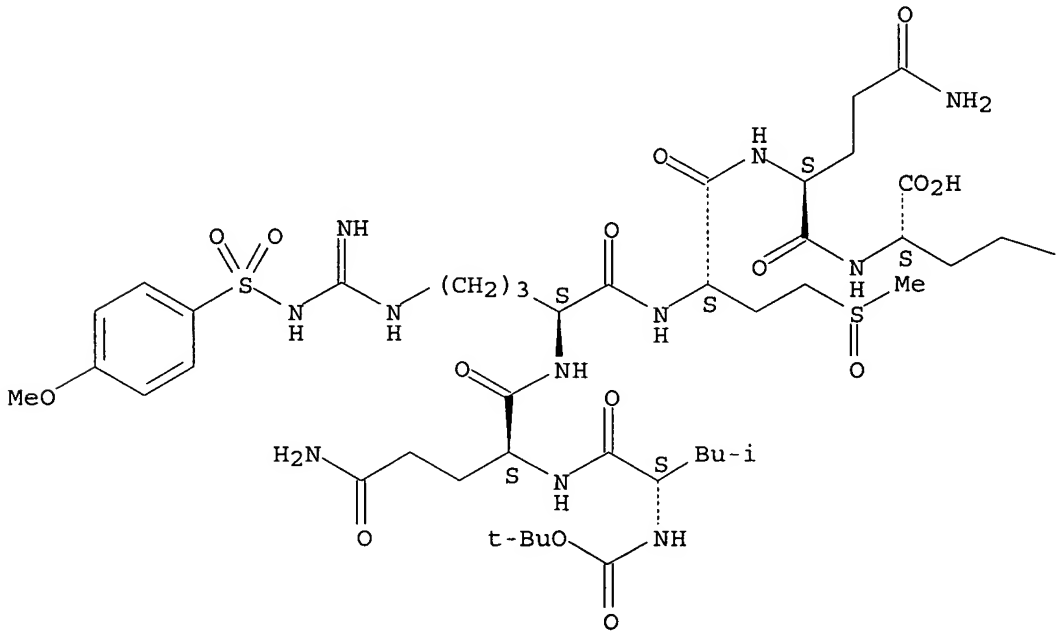
Absolute stereochemistry.



RN 66450-18-8 HCAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-L-glutaminyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, 65-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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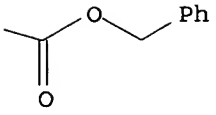
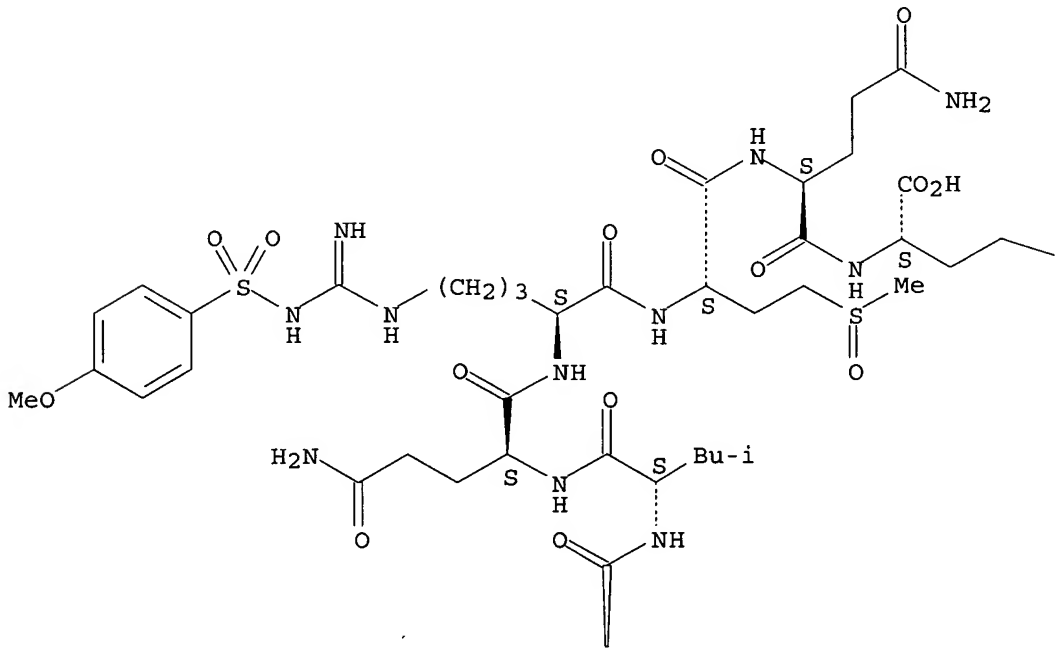


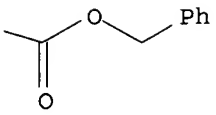
RN 66450-21-3 HCAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-L-α-glutamyl-L-leucyl-L-glutaminyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, 1,75-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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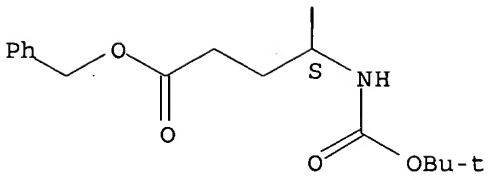
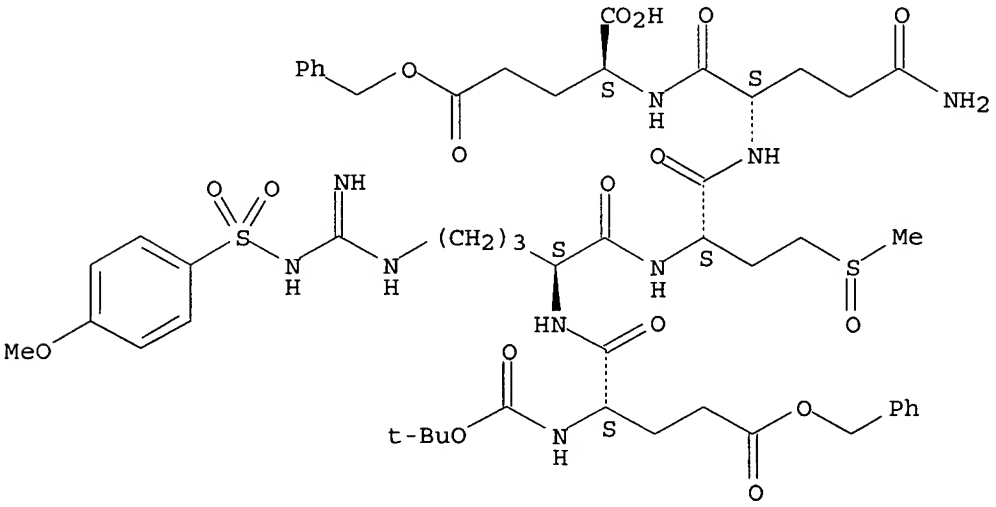


RN 70645-89-5 HCAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, 1,55-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

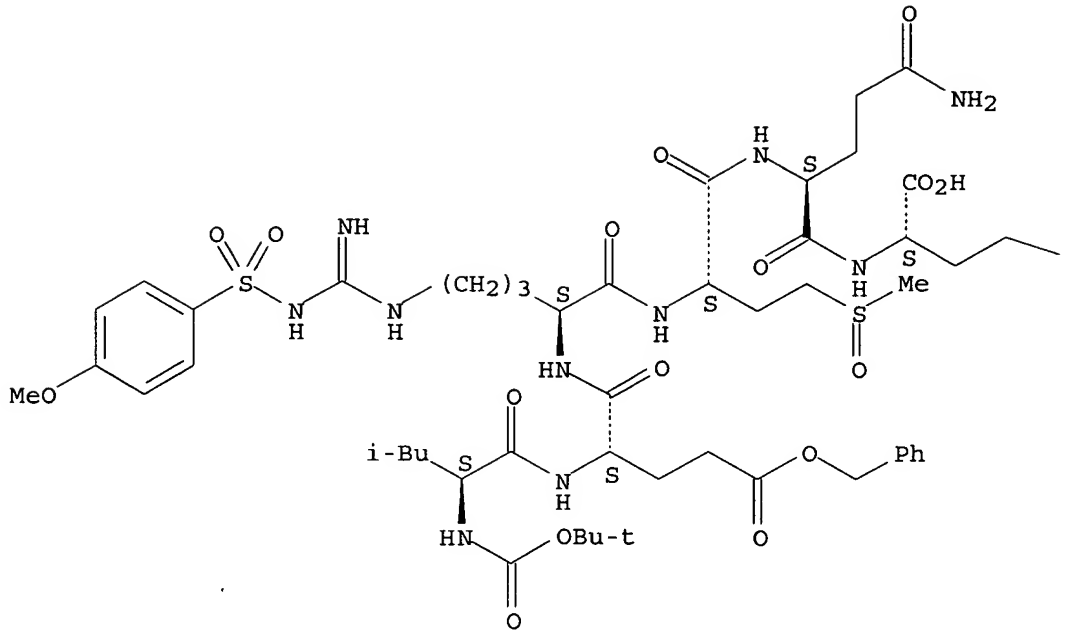
Absolute stereochemistry.



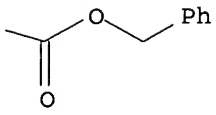
RN 70645-91-9 HCAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, 2,65-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



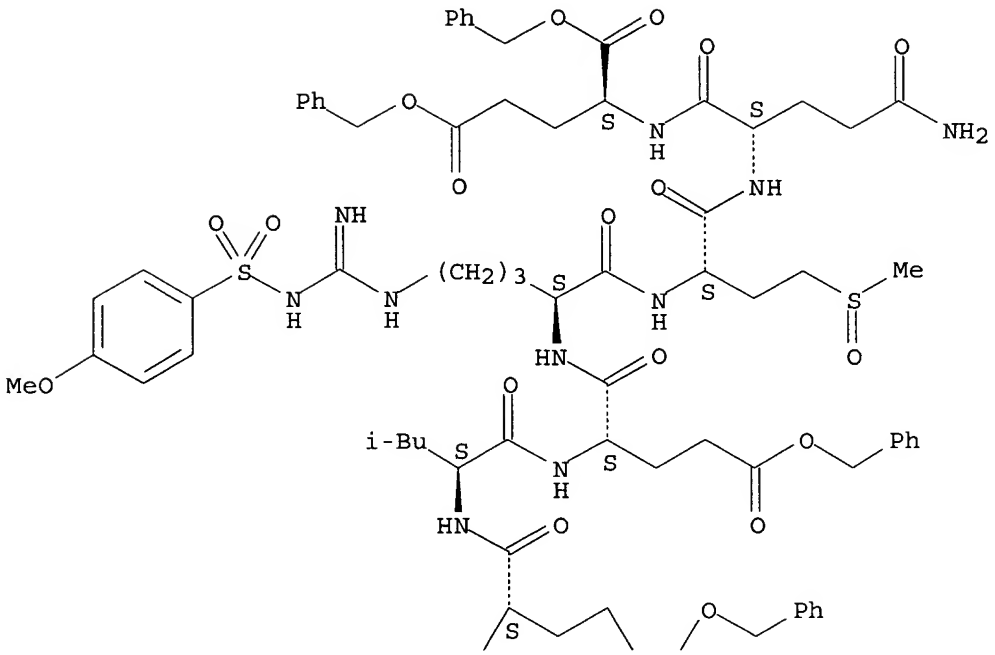
PAGE 1-B



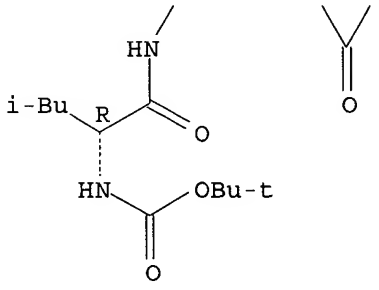
RN 70645-99-7 HCAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-D-leucyl-L-α-glutamyl-L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

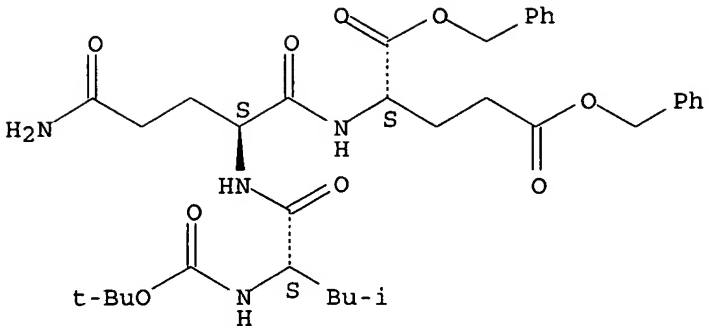


PAGE 2-A



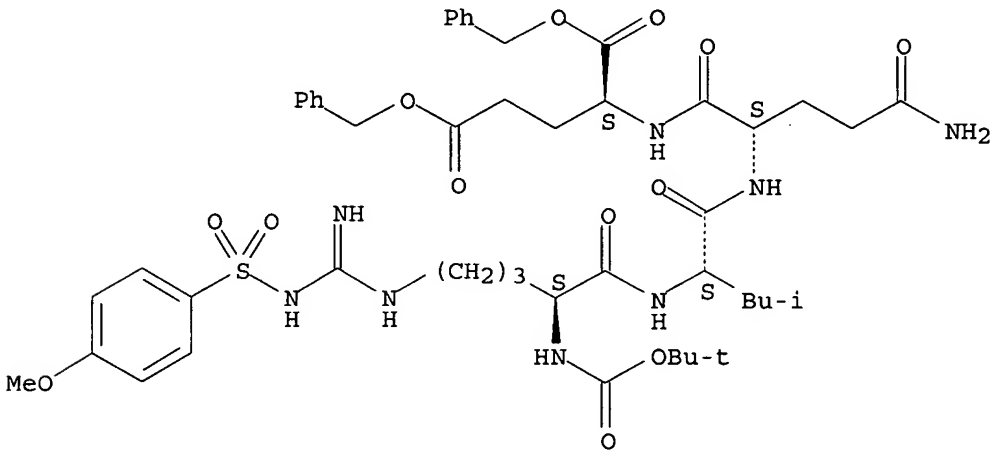
RN 70646-00-3 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl]-L-glutaminyl]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



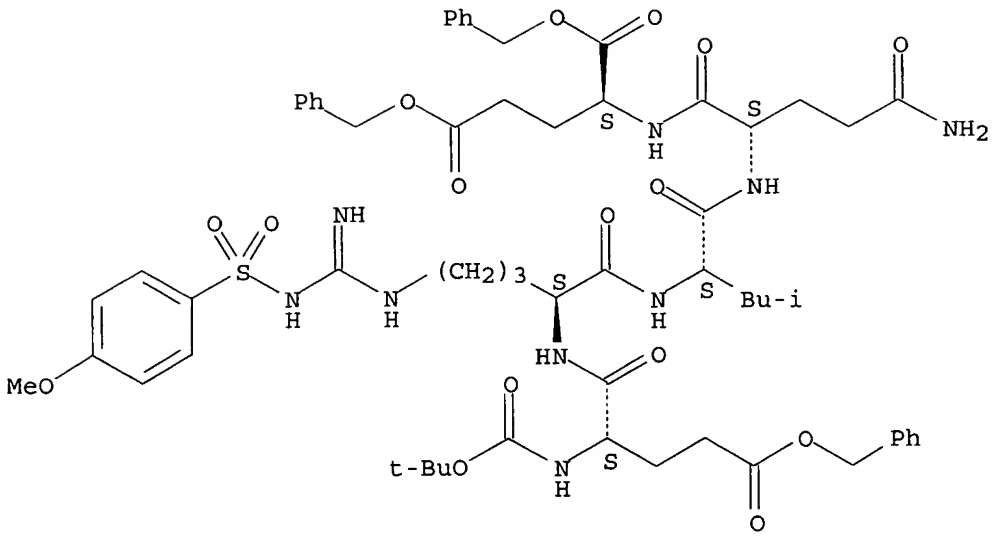
RN 70646-02-5 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[N2-[(1,1-dimethylethoxy)carbonyl]-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-L-leucyl]-L-glutaminyl]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



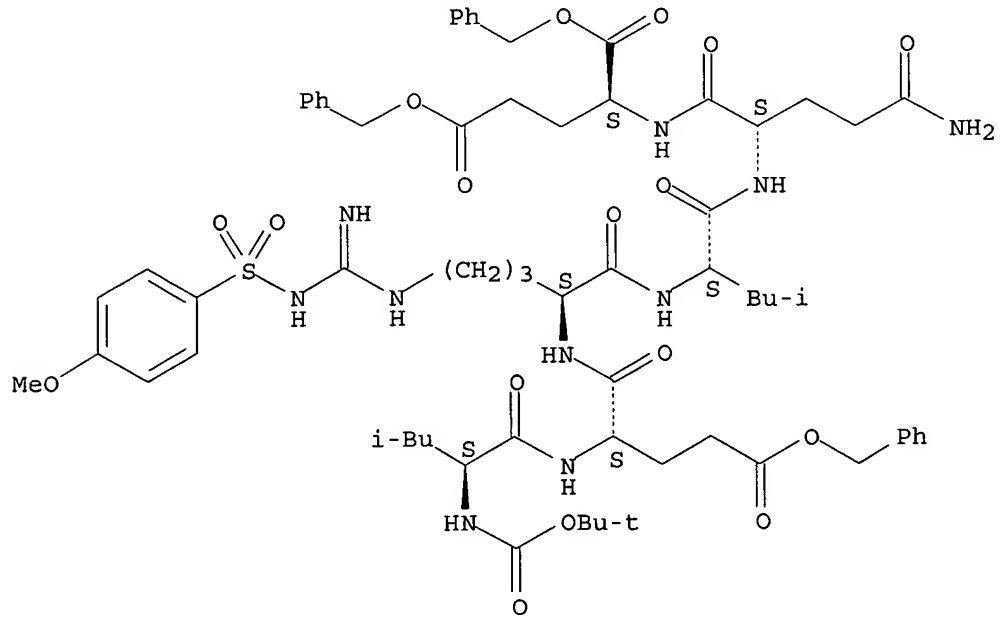
RN 70646-04-7 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[N2-[N-[(1,1-dimethylethoxy)carbonyl]-L-α-glutamyl]-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-L-leucyl]-L-glutaminyl]-, tris(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 70646-06-9 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[N2-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl]-L-α-glutamyl]-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-L-leucyl]-L-glutaminyl]-, tris(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 70646-08-1 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[N2-[N-[N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-D-leucyl]-L-α-glutamyl]-L-leucyl]-L-α-glutamyl]-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-L-leucyl]-L-glutaminyl]-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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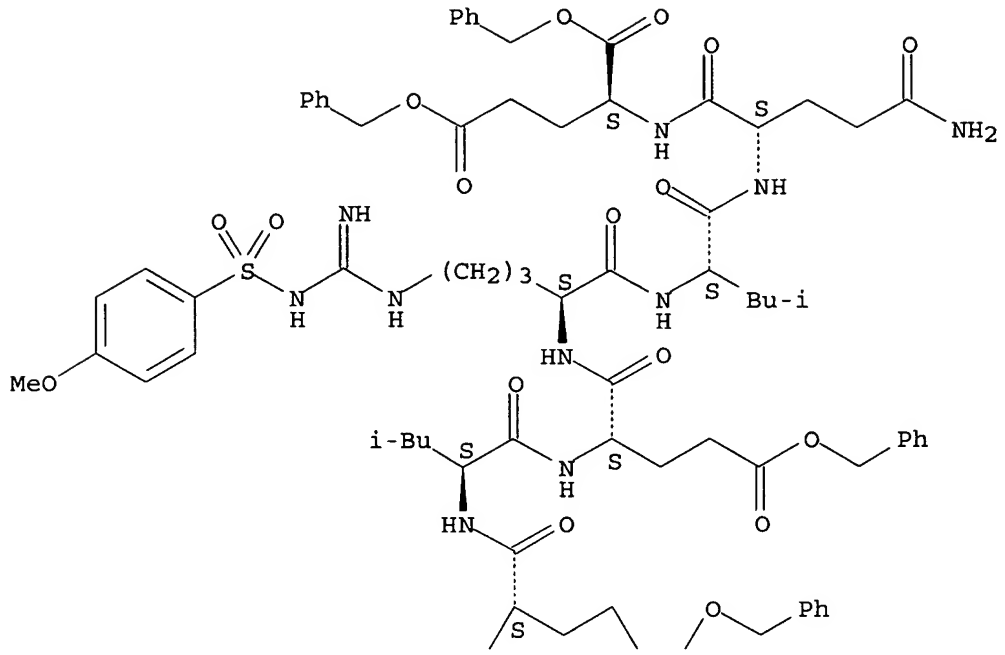

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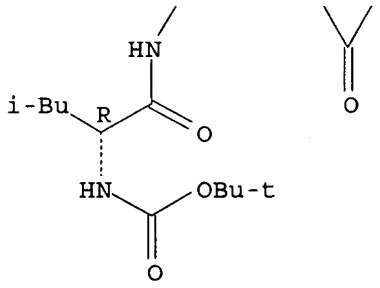
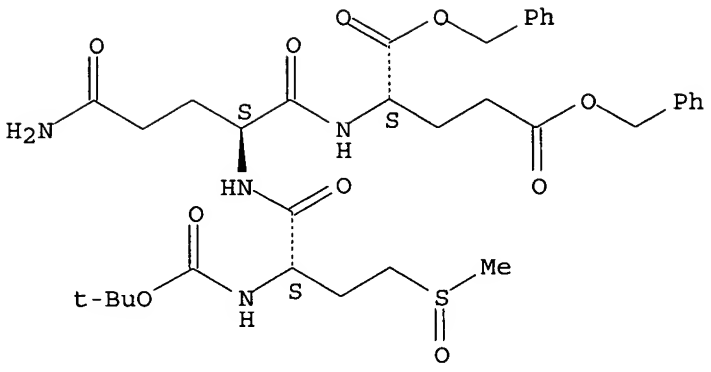


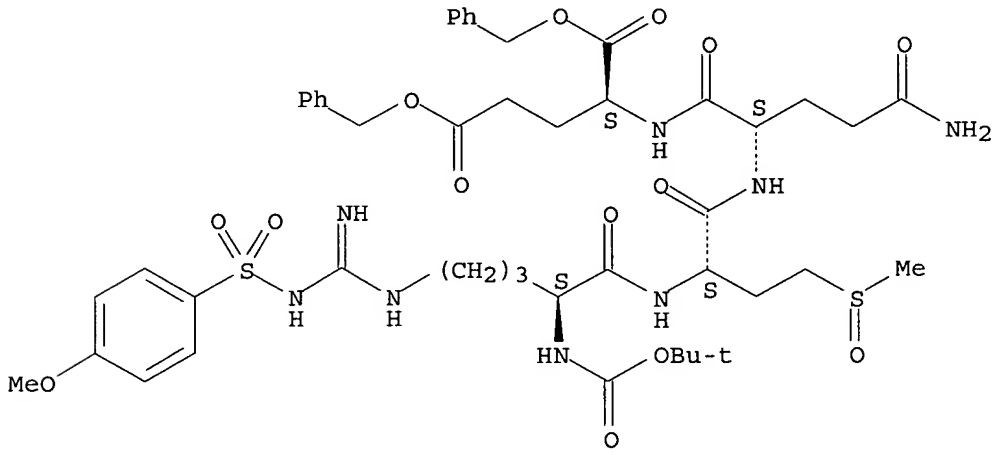
RN 70655-63-9 HCAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



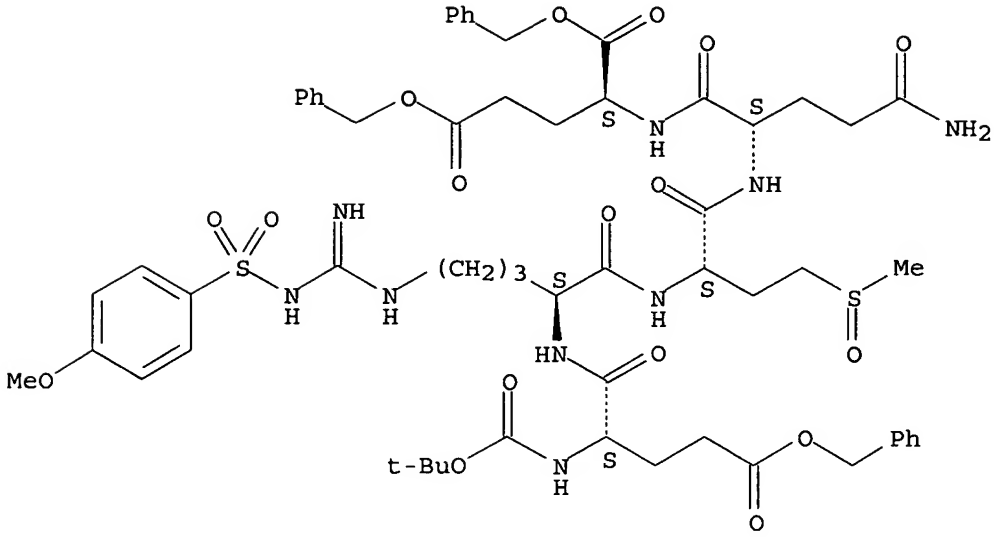
RN 70655-65-1 HCAPLUS
CN L-Glutamic acid, N2-[(1,1-dimethylethoxy)carbonyl]-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



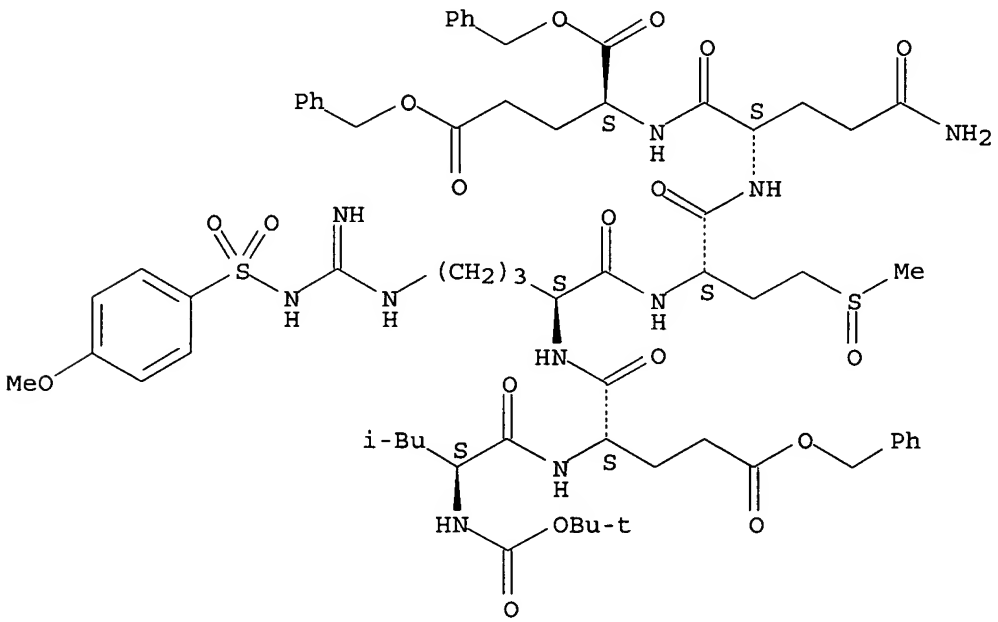
RN 70655-67-3 HCAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, tris(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 70655-69-5 HCAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, tris(phenylmethyl) ester (9CI) (CA INDEX NAME)

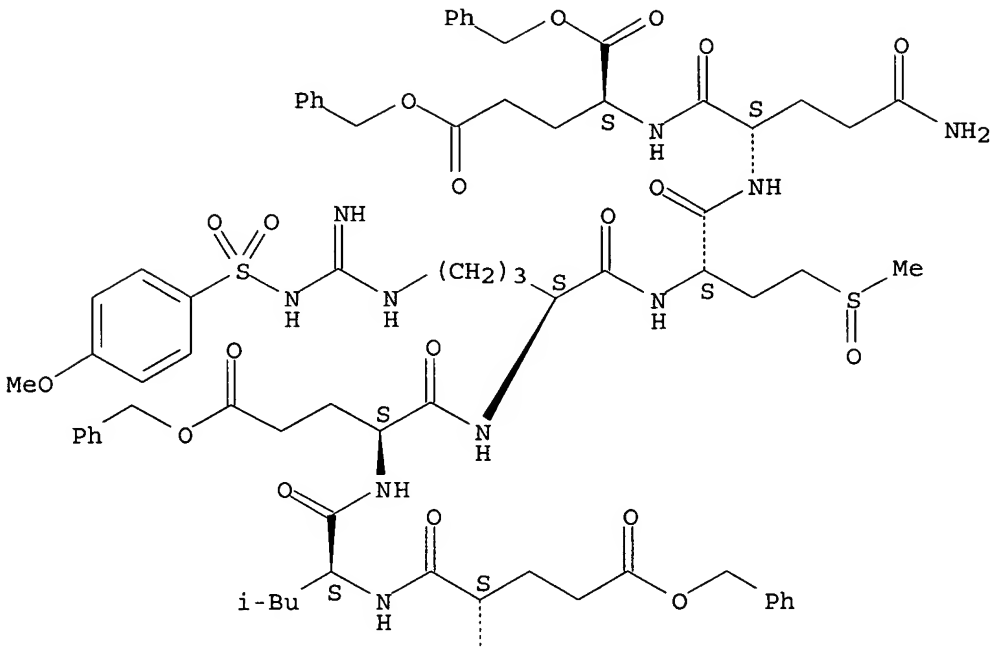
Absolute stereochemistry.



RN 70655-71-9 HCAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-L-α-glutamyl-L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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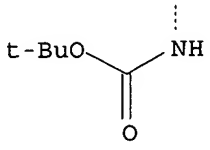
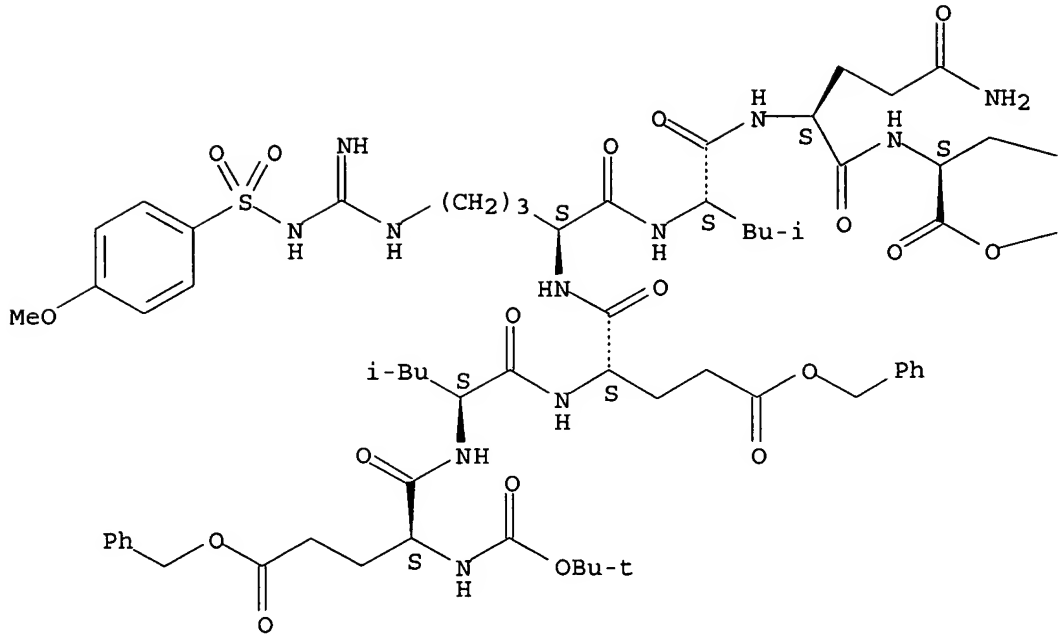


RN 70673-08-4 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[N2-[N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-α-glutamyl]-L-leucyl]-L-α-glutamyl]-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-L-leucyl]-L-glutaminyl]-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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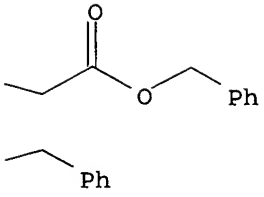
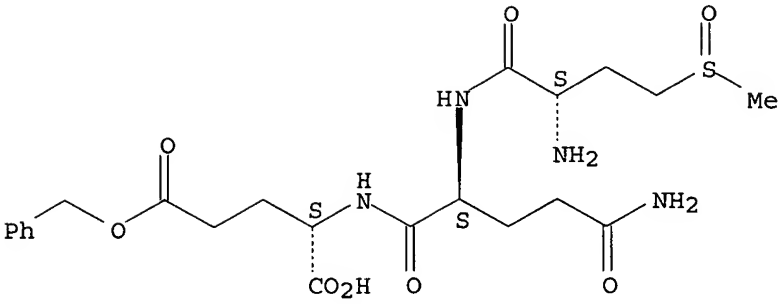


IT **66450-12-2P 70646-01-4P 70655-66-2P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with arginine derivative)
RN 66450-12-2 HCAPLUS
CN L-Glutamic acid, 4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, 35-(phenylmethyl) ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

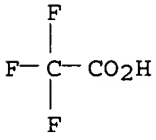
CRN 66450-11-1
CMF C22 H32 N4 O8 S

Absolute stereochemistry.



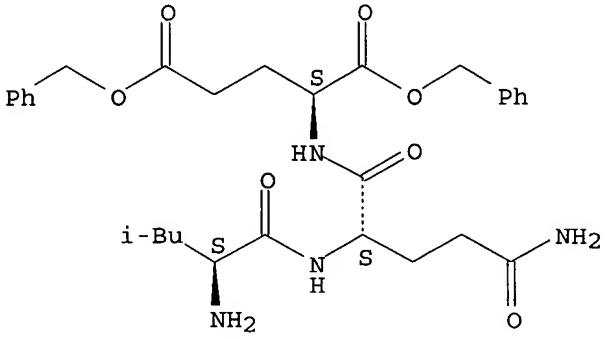
CM 2

CRN 76-05-1
CMF C2 H F3 O2



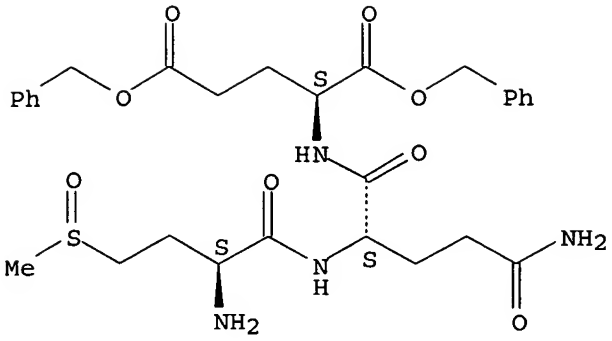
RN 70646-01-4 HCAPLUS
CN L-Glutamic acid, N-(N2-L-leucyl-L-glutaminyl)-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 70655-66-2 HCAPLUS
CN L-Glutamic acid, 4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **70645-82-8P 70645-85-1P 70645-92-0P**
70646-03-6P 70655-70-8P 70673-07-3P
70686-48-5P
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with glutamic acid derivative)

RN 70645-82-8 HCAPLUS

CN L-Glutamic acid, L-leucyl-L-glutaminyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, 65-(phenylmethyl) ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 70645-81-7
CMF C46 H69 N11 O15 S2

Absolute stereochemistry.

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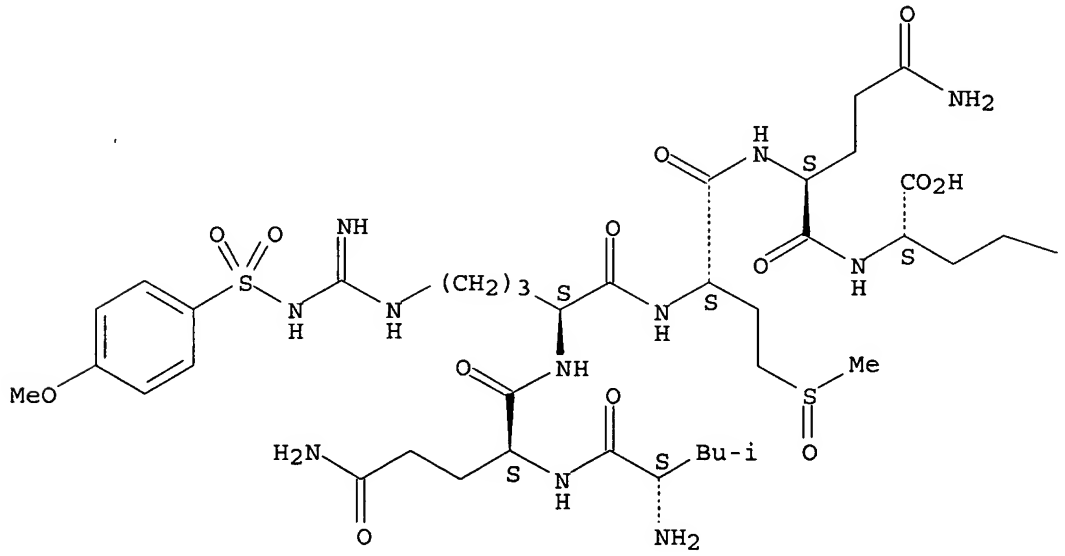

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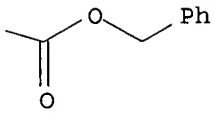
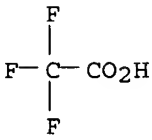


CM 2

CRN 76-05-1
CMF C2 H F3 O2



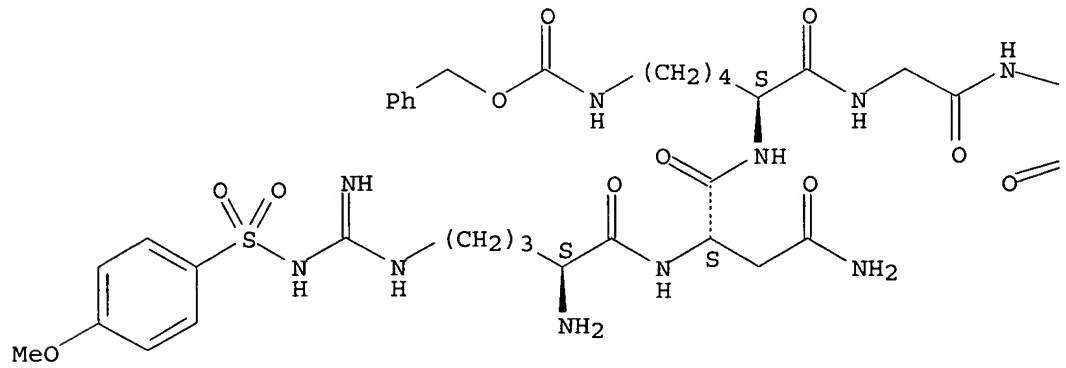
RN 70645-85-1 HCAPLUS
CN L-Glutamic acid, N-[N-[N2-[N2-[N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-L-asparaginyl]-N6-[(phenylmethoxy)carbonyl]-L-lysyl]glycyl]-, 1-(phenylmethyl) ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 70645-84-0
CMF C45 H60 N10 O14 S

Absolute stereochemistry.

PAGE 1-A



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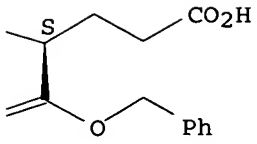
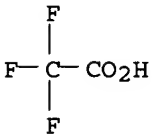


CM 2

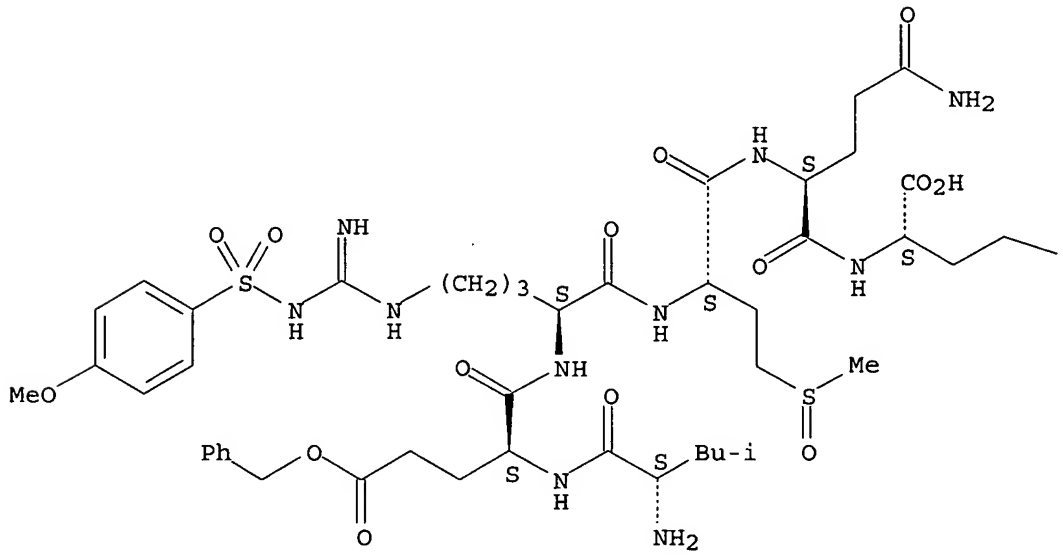
CRN 76-05-1
CMF C2 H F3 O2

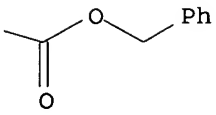


RN 70645-92-0 HCAPLUS
CN L-Glutamic acid, L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, 2,65-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

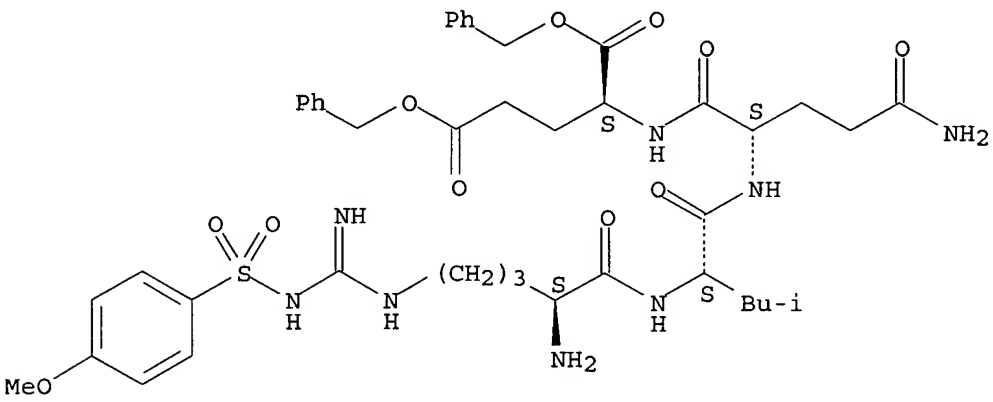
PAGE 1-A





RN 70646-03-6 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-L-leucyl]-L-glutaminyl]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

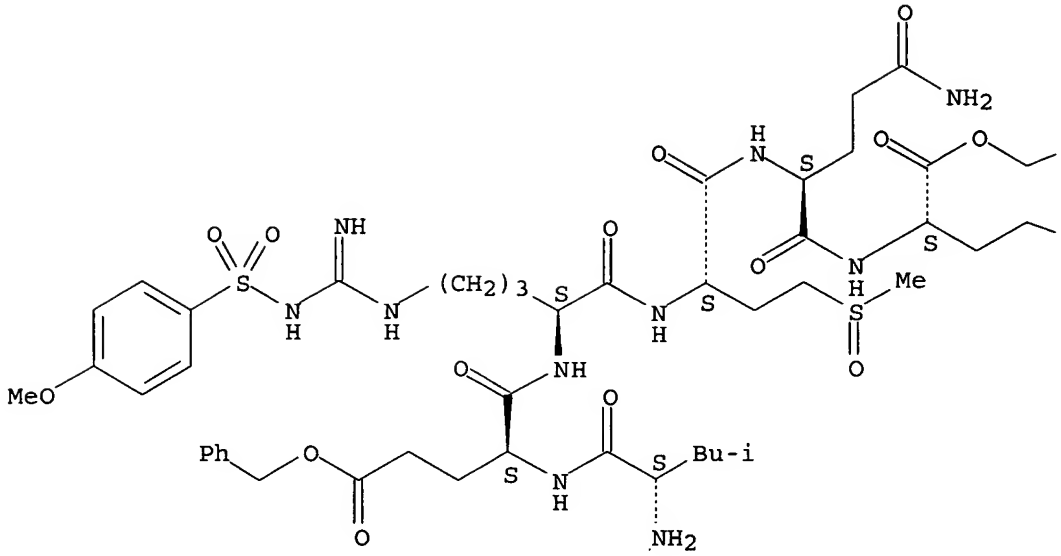
Absolute stereochemistry.



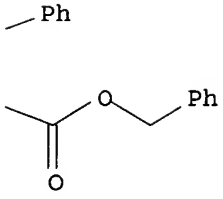
RN 70655-70-8 HCAPLUS
CN L-Glutamic acid, L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, tris(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

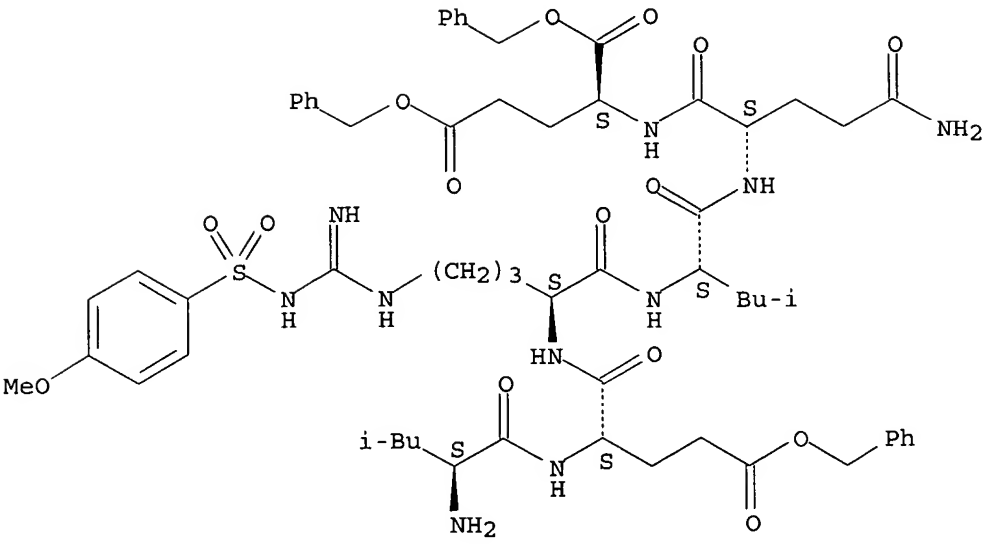


PAGE 1-B



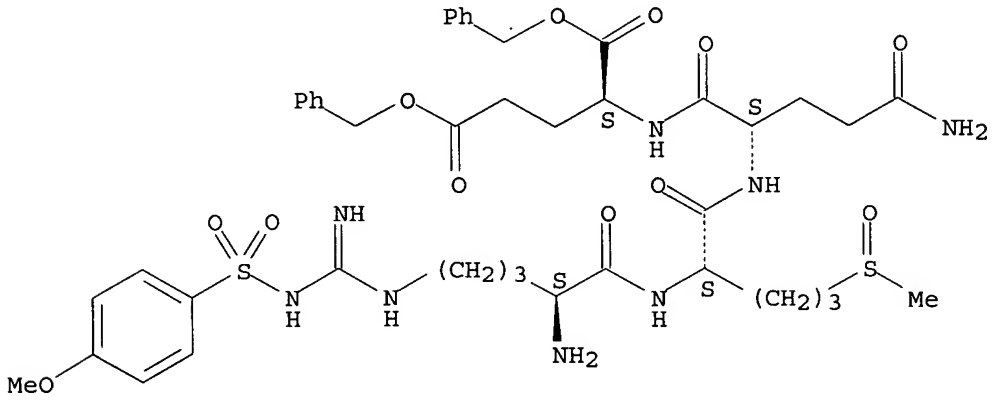
RN 70673-07-3 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-N2-(N-L-leucyl-L-α-glutamyl)-L-ornithyl]-L-leucyl]-L-glutaminyl]-, tris(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 70686-48-5 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-5-(methylsulfinyl)-L-norvalyl]-L-glutaminyl]-, bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



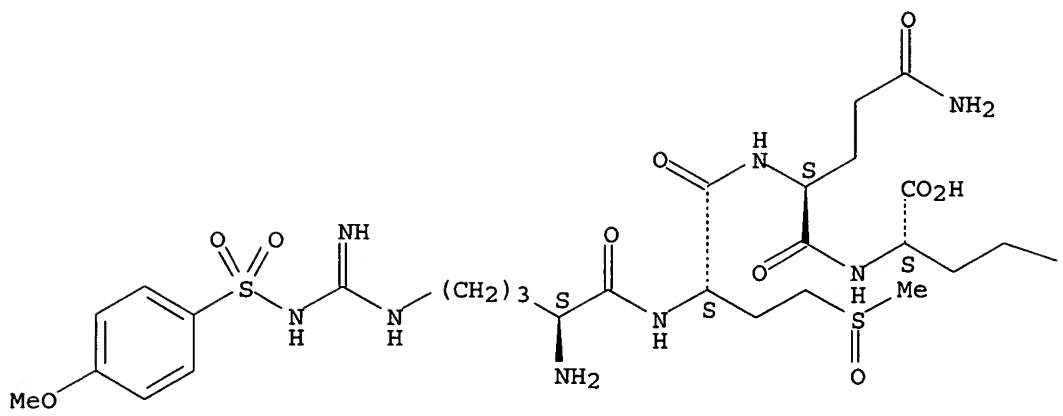
IT **66450-15-5P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with glutamine derivative)
RN 66450-15-5 HCAPLUS
CN L-Glutamic acid, N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, 45-(phenylmethyl) ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 66450-14-4
CMF C35 H50 N8 O12 S2

Absolute stereochemistry.

PAGE 1-A



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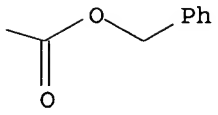
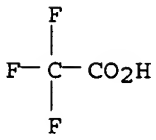


CM 2

CRN 76-05-1
CMF C2 H F3 O2

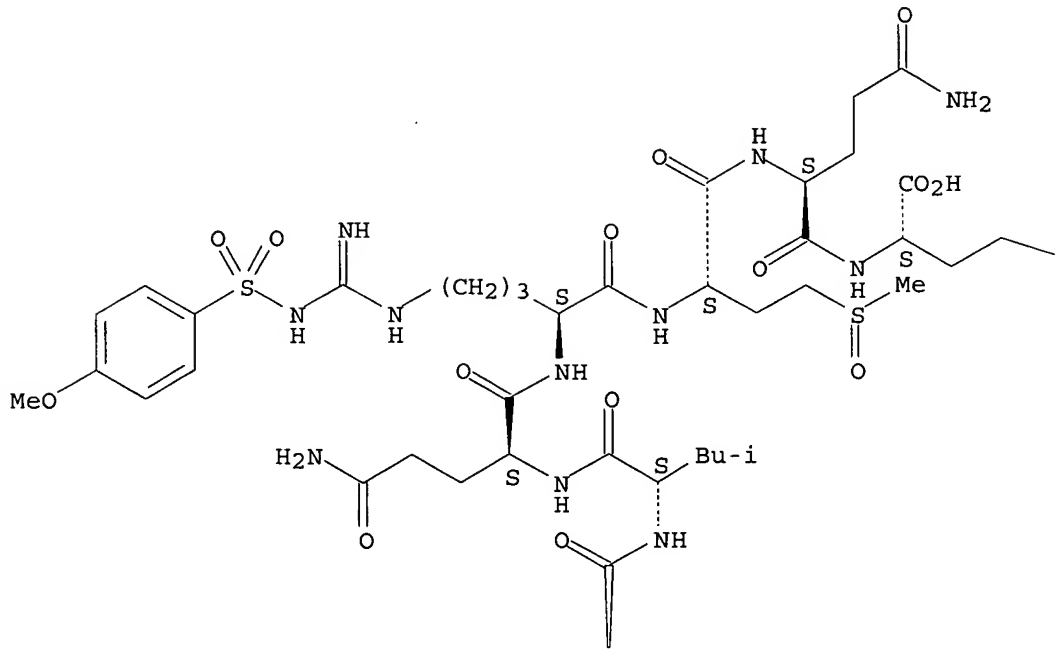


IT **66714-36-1P 70645-93-1P 70646-09-2P**
70646-12-7P 70646-18-3P
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with heptapeptide derivative)
RN 66714-36-1 HCAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-D-alanyl-L-α-glutamyl-L-leucyl-L-glutaminyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-,

2,85-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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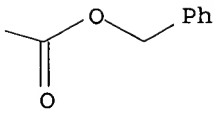
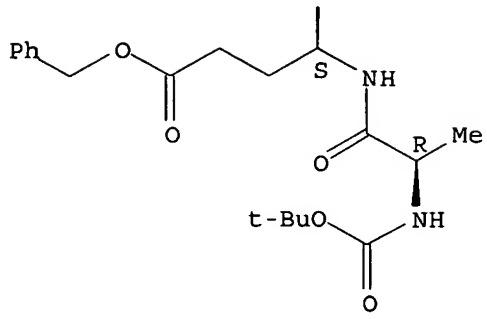


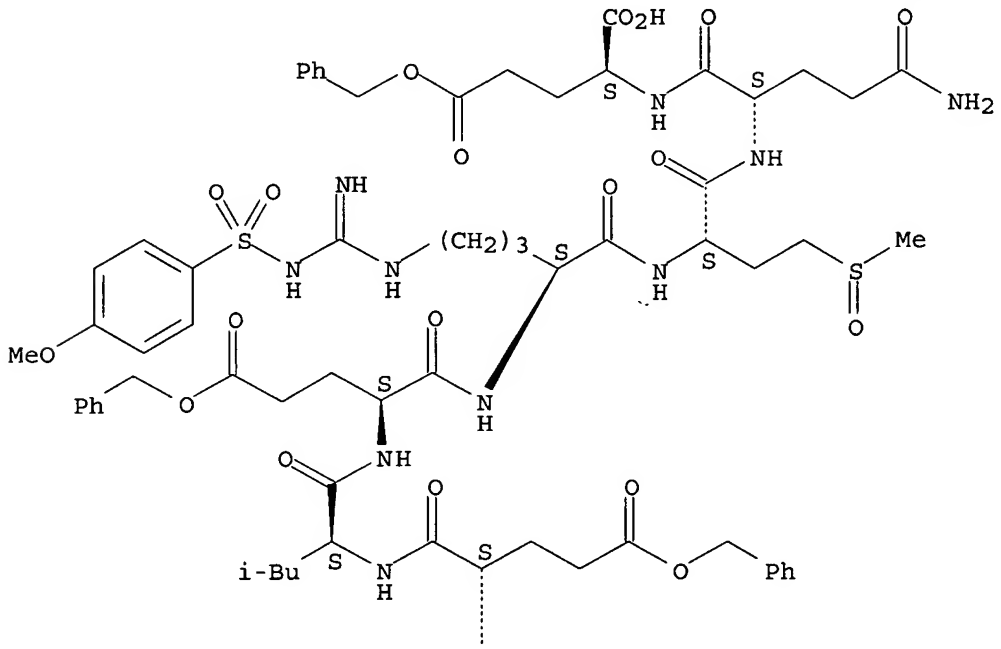
PAGE 2-A



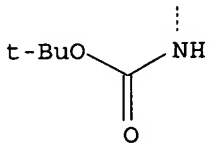
RN 70645-93-1 HCAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-L-α-glutamyl-L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, 1,3,75-tris(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



RN 70646-09-2 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-N2-[N-[N-(N-D-leucyl-L-α-glutamyl)-L-leucyl]-L-α-glutamyl]-L-ornithyl]-L-leucyl]-L-glutaminyl]-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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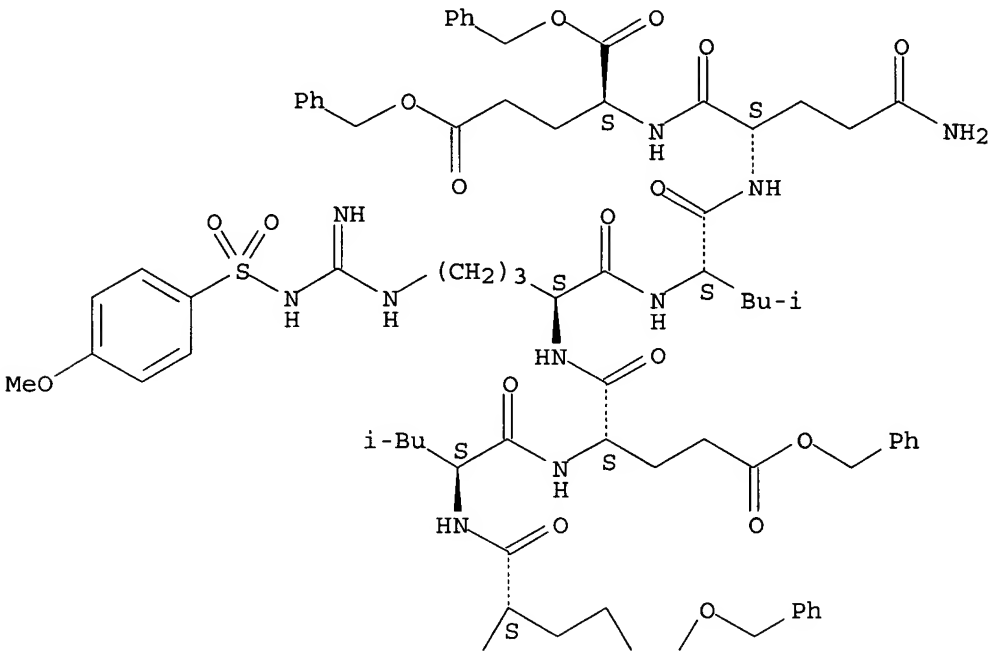

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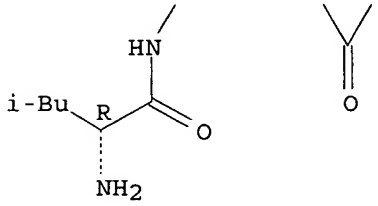
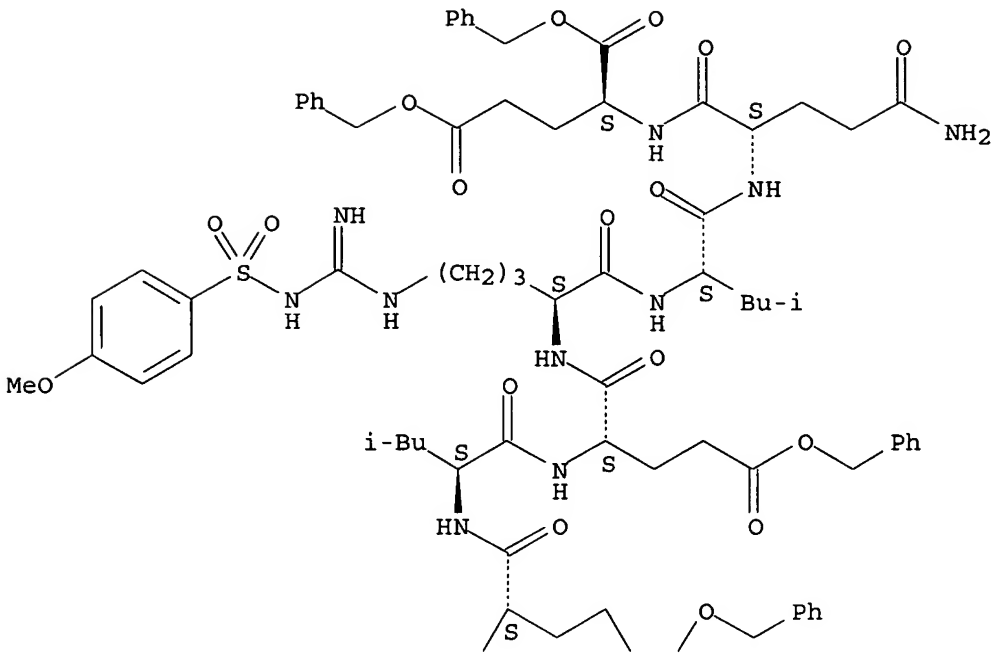


RN 70646-12-7 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[N2-[N-[N-(N-D-alanyl-L-α-glutamyl)-L-leucyl]-L-α-glutamyl]-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-L-leucyl]-L-glutaminyl]-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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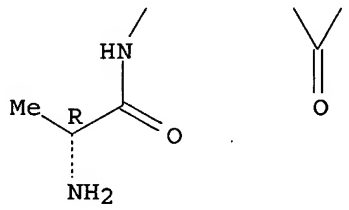
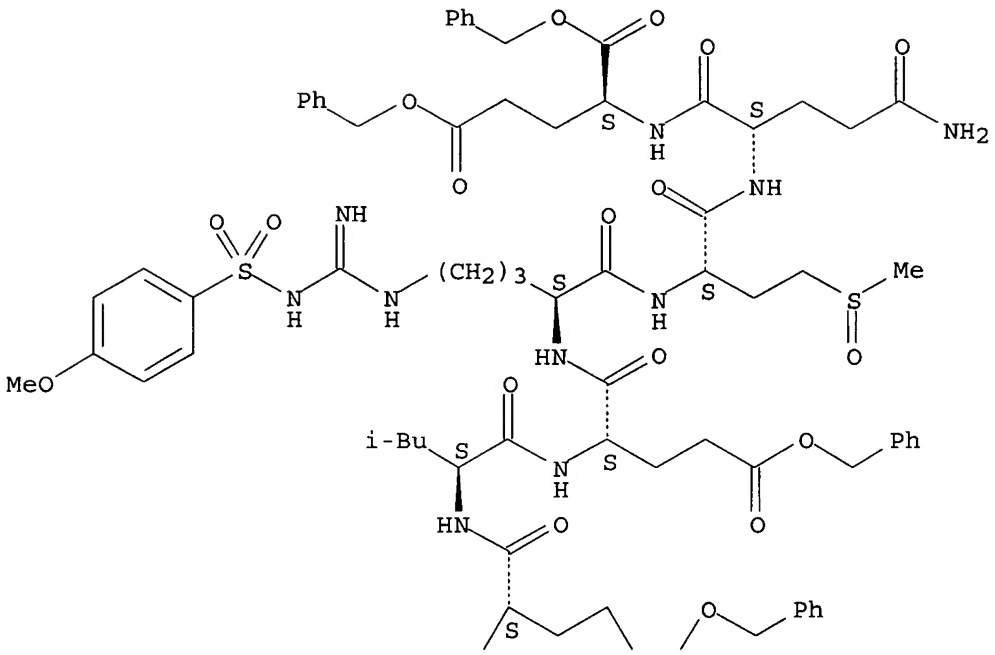


RN 70646-18-3 HCAPLUS
CN L-Glutamic acid, D-alanyl-L-α-glutamyl-L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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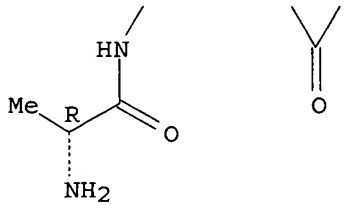
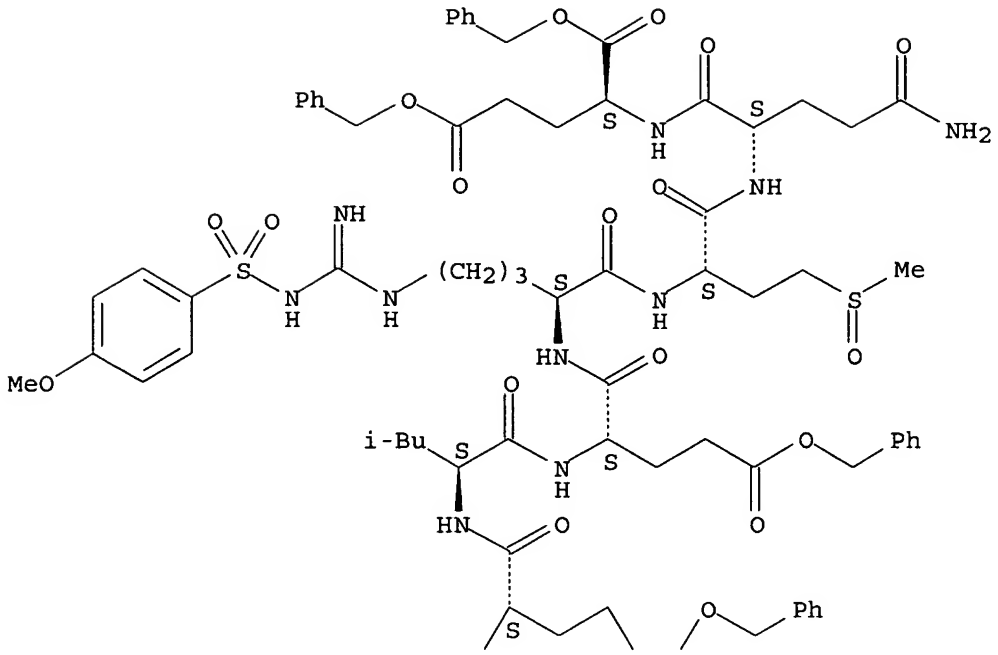


IT **70646-26-3P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with heptapeptides derivative)
RN 70646-26-3 HCAPLUS
CN L-Glutamic acid, D-leucyl-L-α-glutamyl-L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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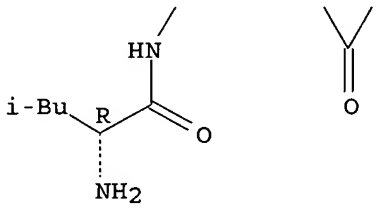


IT **66517-90-6P 70645-90-8P 70646-05-8P**
70655-68-4P
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with leucine derivative)

RN 66517-90-6 HCAPLUS

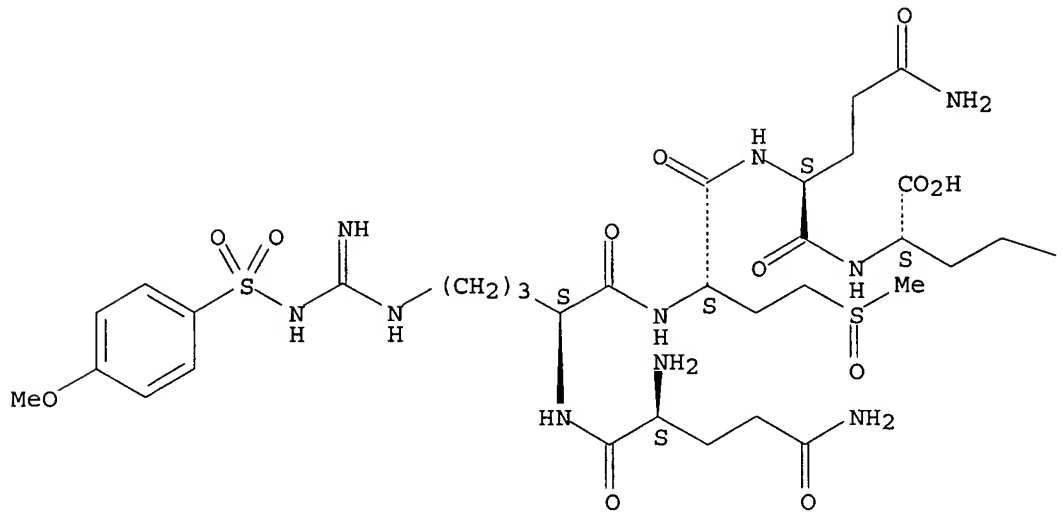
CN L-Glutamic acid, L-glutaminyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, 55-(phenylmethyl) ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 66517-89-3
CMF C40 H58 N10 O14 S2

Absolute stereochemistry.

PAGE 1-A



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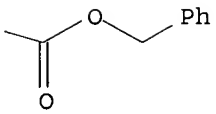
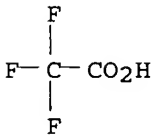


CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 70645-90-8 HCAPLUS
CN L-Glutamic acid, L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, 1,55-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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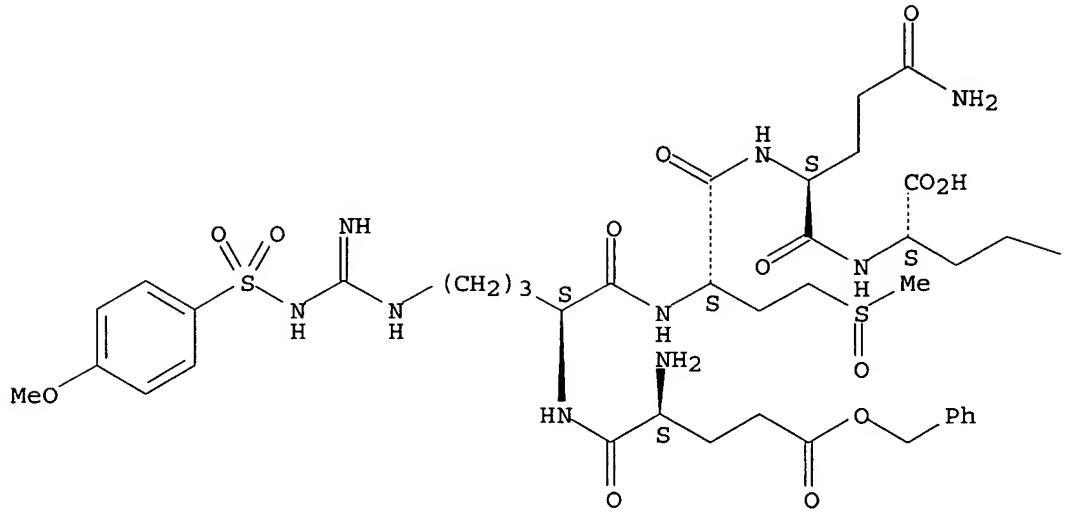

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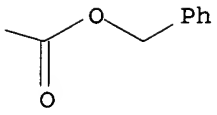
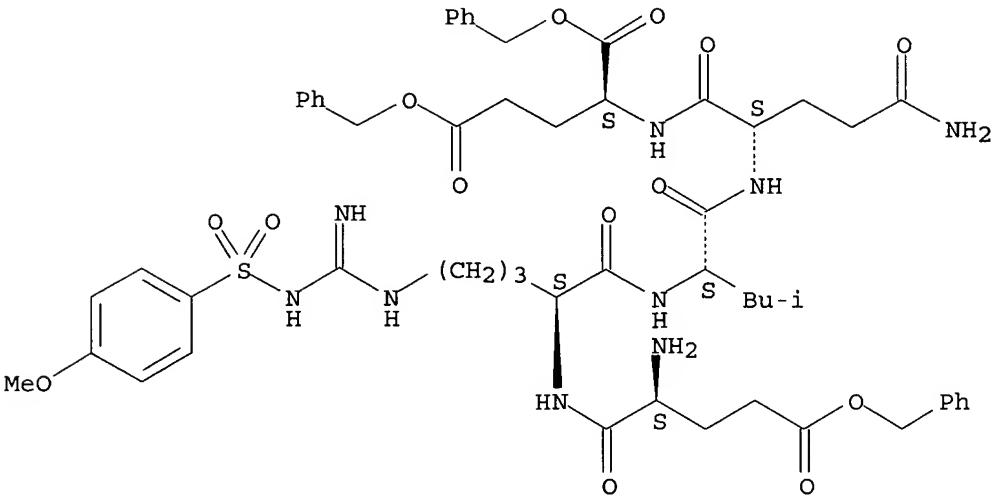


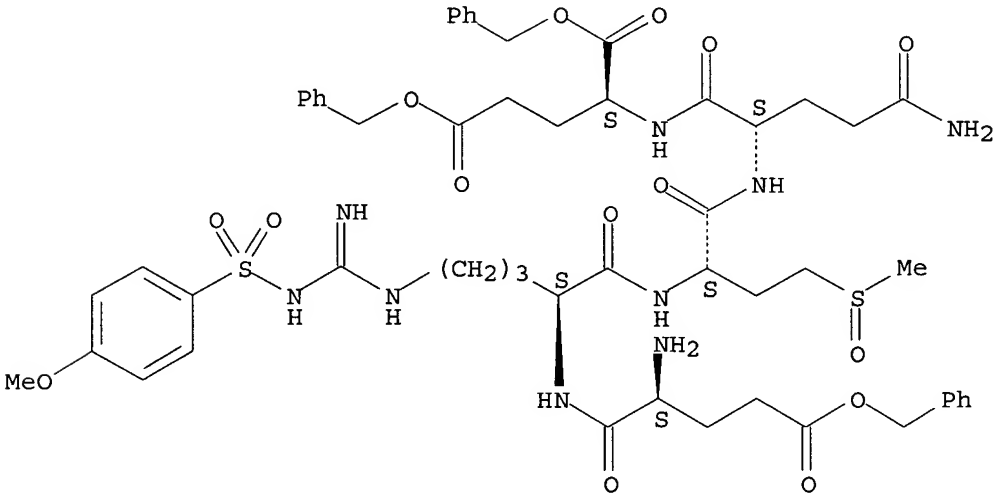
RN 70646-05-8 HCAPLUS
CN L-Glutamic acid, N-[N2-[N-[N2-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-L-leucyl]-L-glutaminyl]-, tris(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 70655-68-4 HCAPLUS
CN L-Glutamic acid, L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, tris(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **66450-19-9P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with octapeptide derivative)
RN 66450-19-9 HCAPLUS
CN L-Glutamic acid, L-α-glutamyl-L-leucyl-L-glutaminyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, 1,75-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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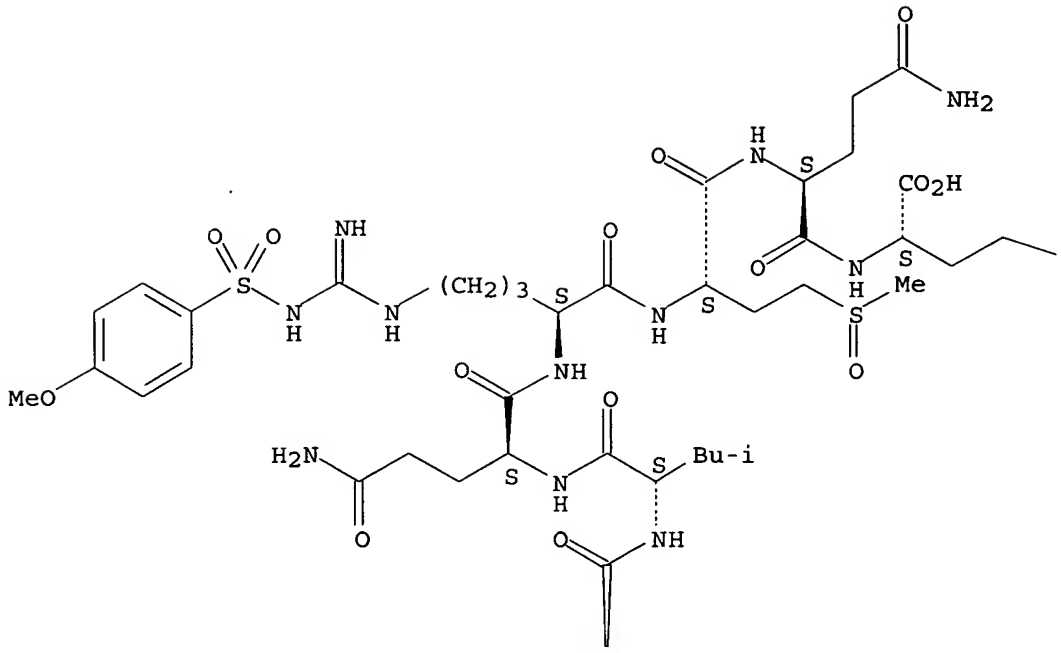

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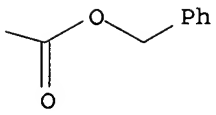

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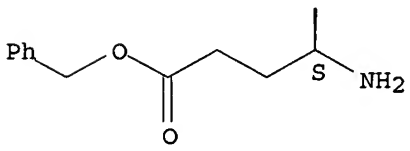
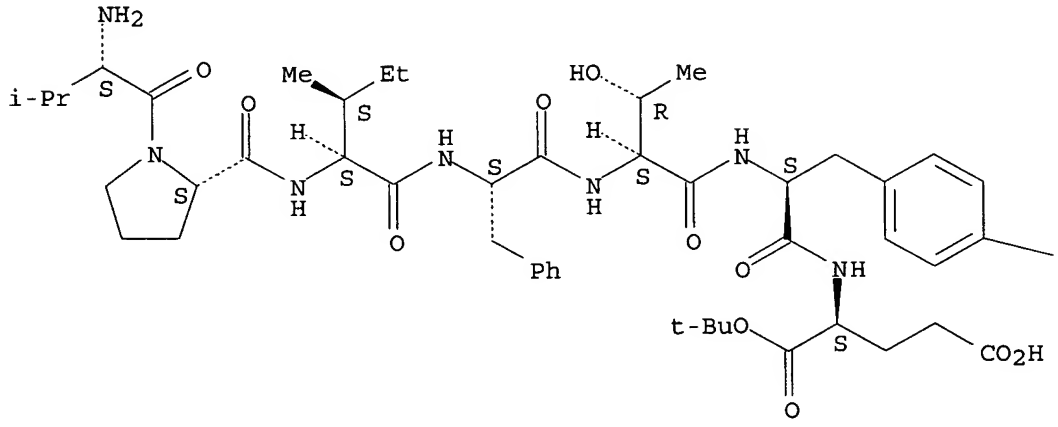


IT **70645-78-2P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with phenylalanine derivative)
RN 70645-78-2 HCAPLUS

CN L-Glutamic acid, N-[N-[N-[N-[N-(1-L-valyl-L-prolyl)-L-isoleucyl]-L-phenylalanyl]-L-threonyl]-L-tyrosyl]-, 1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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—OH

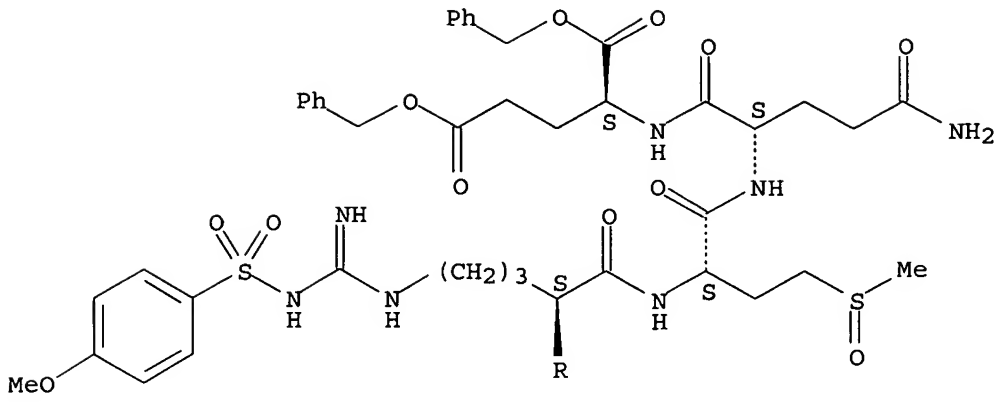
IT **70655-72-0P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with D-alanine derivative)

RN 70655-72-0 HCAPLUS

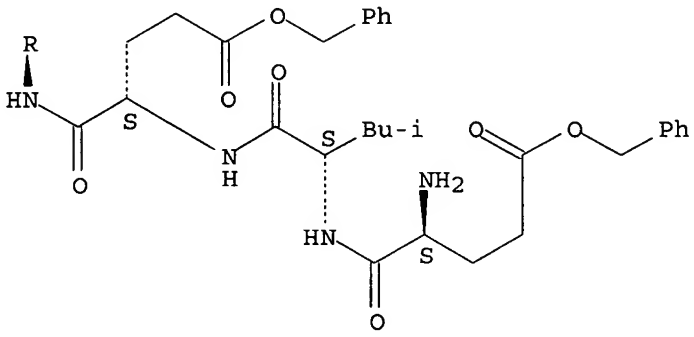
CN L-Glutamic acid, L-α-glutamyl-L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



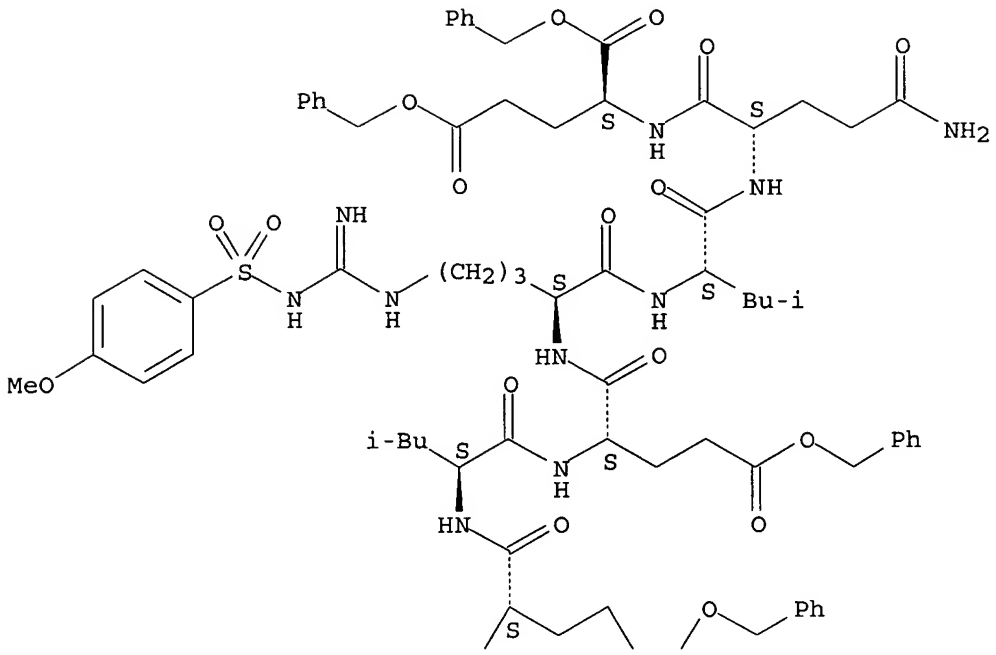
IT **70646-07-0P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with D-leucine derivative)

RN 70646-07-0 HCAPLUS

CN L-Glutamic acid, N-[N2-[N-[N2-[N-(N-L-α-glutamyl-L-leucyl)-L-α-glutamyl]-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl]-L-leucyl]-L-glutaminyl]-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

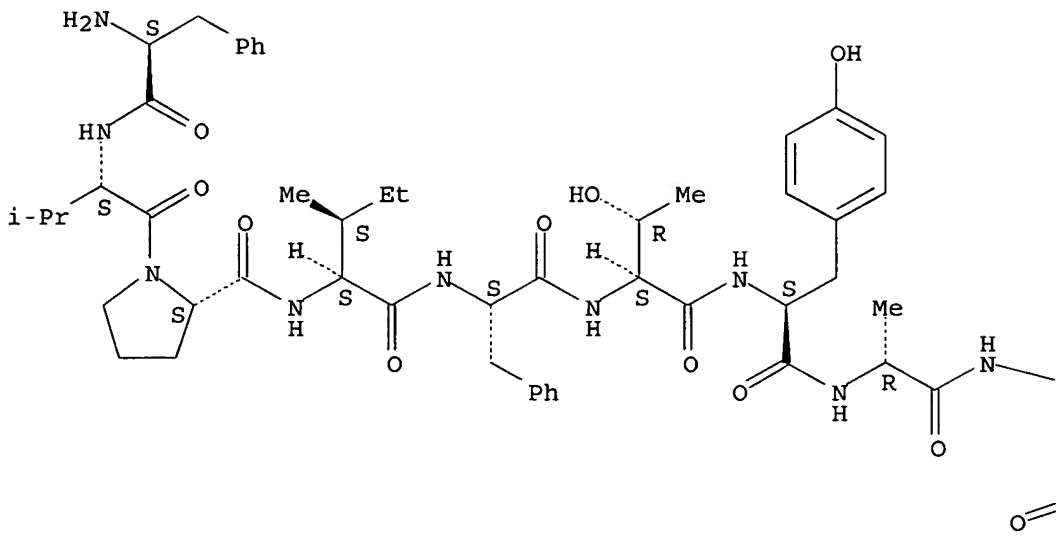


PAGE 2-A

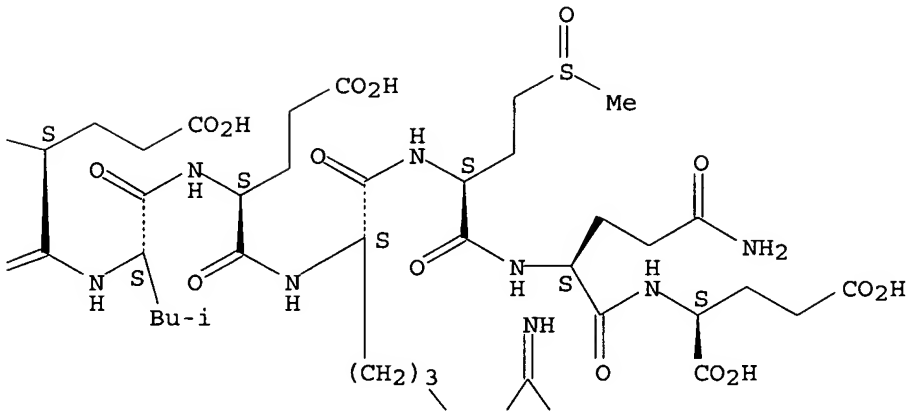
IT **70646-20-7P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and **reductive** cleavage of)
RN 70646-20-7 HCAPLUS
CN Motilin (swine), 8-D-alanine-11-L-glutamic acid-13-[4-(methylsulfinyl)-L-2-aminobutanoic acid]-16-de-L-lysine-17-de-L-glutamic acid-18-de-L-arginine-19-de-L-asparagine-20-de-L-lysine-21-deglycine-22-de-L-glutamine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

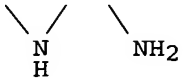
PAGE 1-A



PAGE 1-B



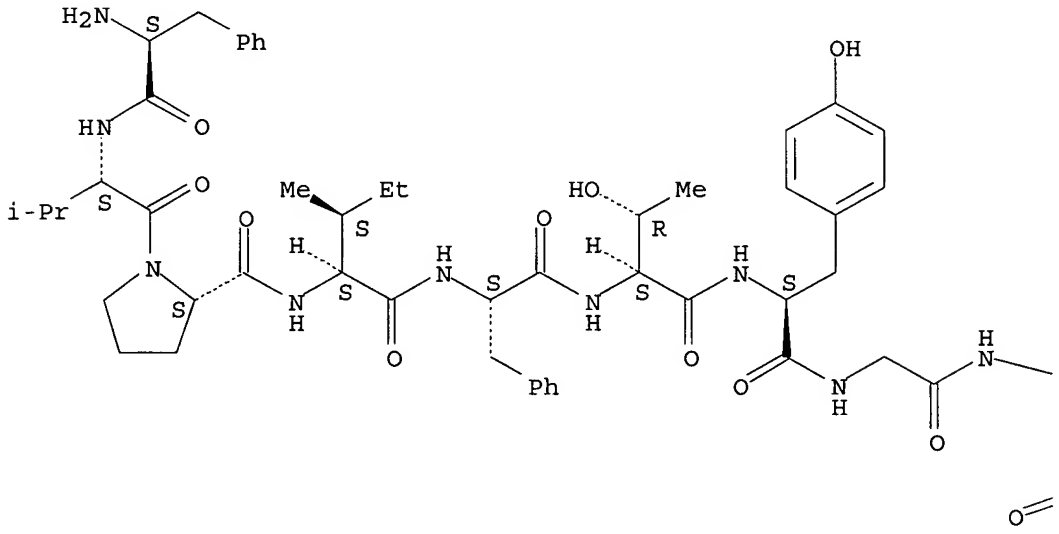
PAGE 2-B



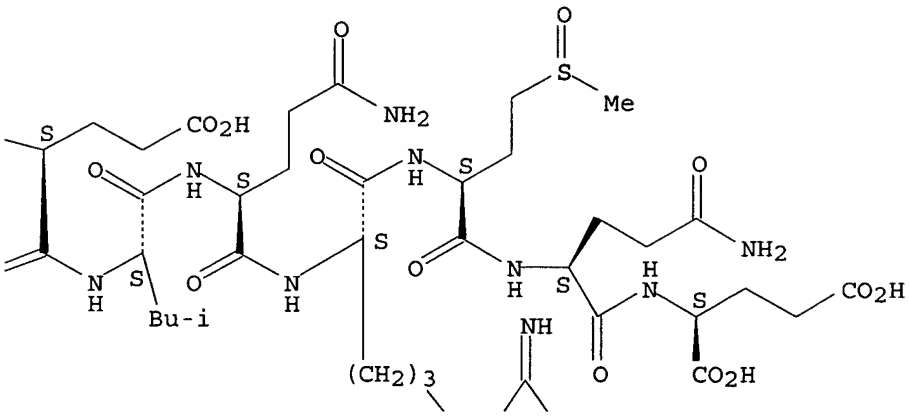
IT **70645-87-3P 70646-16-1P**
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation and **reductive** deblocking of)
RN 70645-87-3 HCAPLUS
CN Motilin (swine), 13-[4-(methylsulfinyl)-L-2-aminobutanoic acid]-16-de-L-lysine-17-de-L-glutamic acid-18-de-L-arginine-19-de-L-asparagine-20-de-L-lysine-21-deglycine-22-de-L-glutamine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

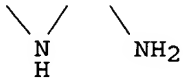
PAGE 1-A



PAGE 1-B



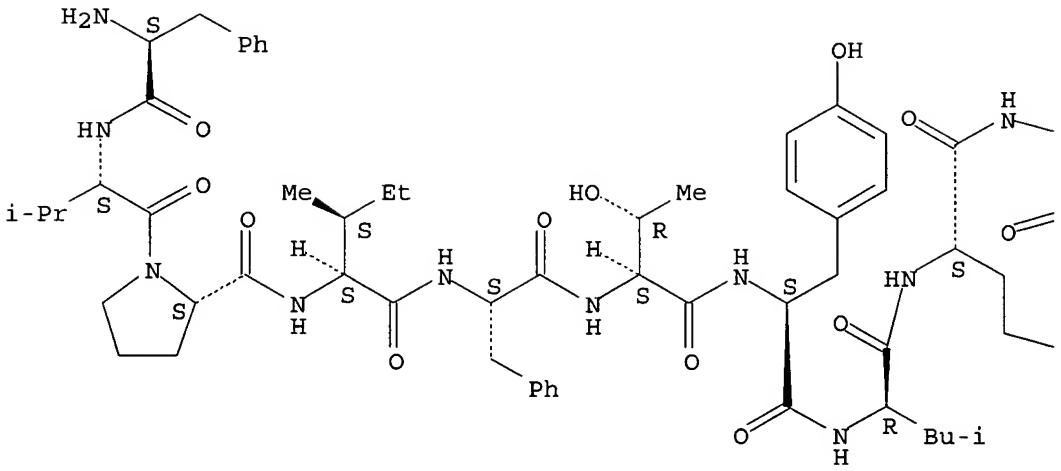
PAGE 2-B



RN 70646-16-1 HCAPLUS
CN Motilin (swine), 8-D-leucine-11-L-glutamic acid-13-[4-(methylsulfinyl)-L-2-aminobutanoic acid]-16-de-L-lysine-17-de-L-glutamic acid-18-de-L-arginine-19-de-L-asparagine-20-de-L-lysine-21-deglycine-22-de-L-glutamine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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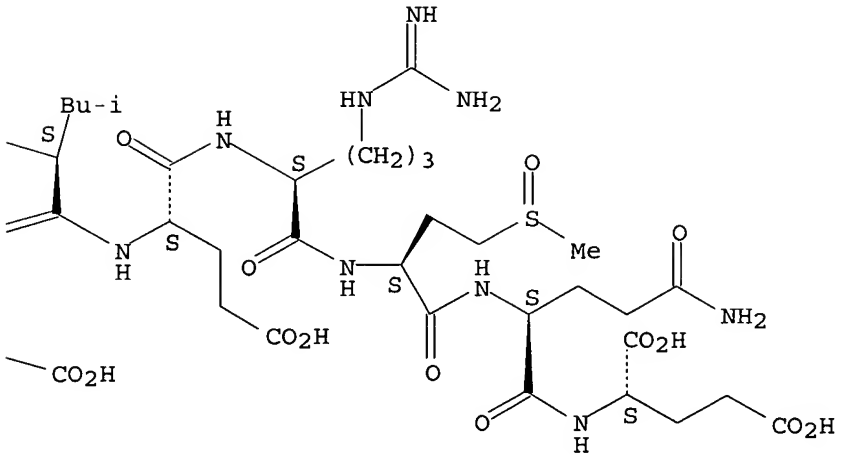
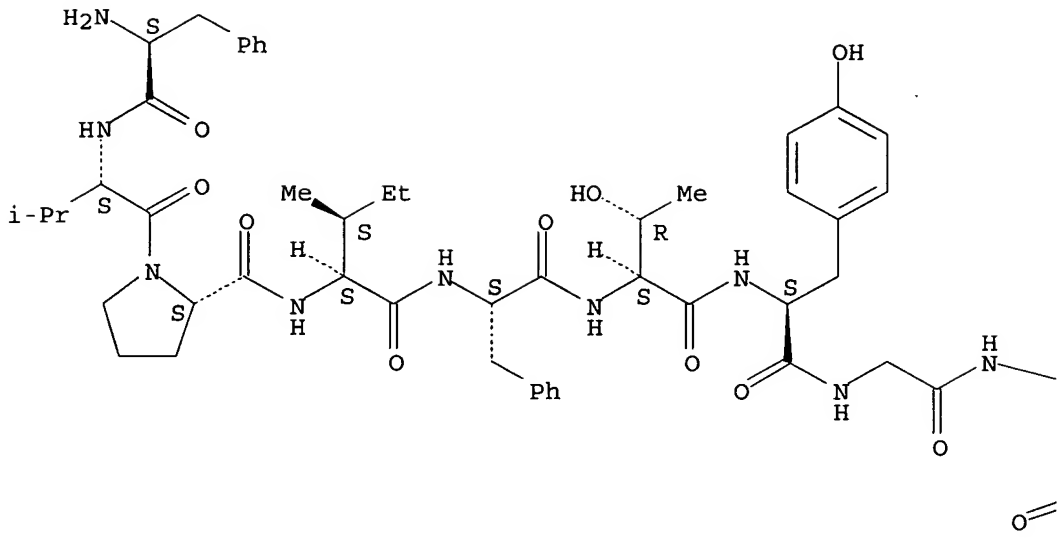


IT **70645-88-4P 70645-98-6P 70646-11-6P**
70646-14-9P 70646-17-2P 70646-21-8P
70646-23-0P 70646-24-1P 70646-25-2P
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation of)
RN 70645-88-4 HCAPLUS
CN Motilin (swine), 12-de-L-arginine-16-de-L-lysine-17-de-L-glutamic acid-18-de-L-arginine-19-de-L-asparagine-20-de-L-lysine-21-deglycine-22-de-L-glutamine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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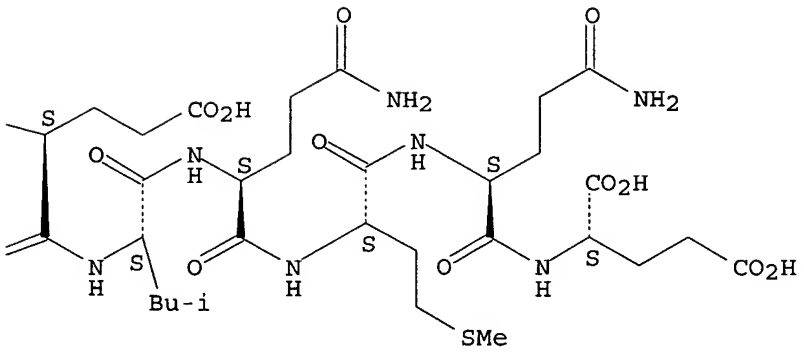
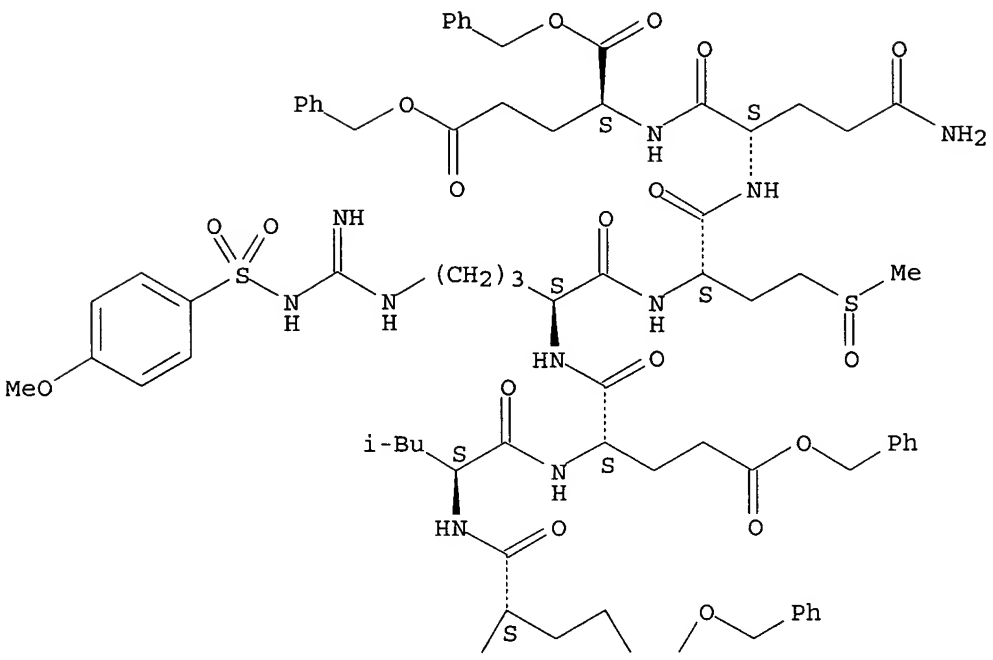


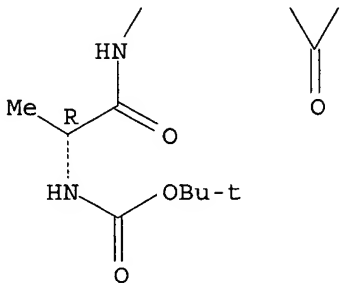
RN 70645-98-6 HCAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-D-alanyl-L-α-glutamyl-L-leucyl-L-α-glutamyl-N5-[imino[[(4-methoxyphenyl)sulfonyl]amino]methyl]-L-ornithyl-4-(methylsulfinyl)-L-2-aminobutanoyl-L-glutaminyl-, tetrakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



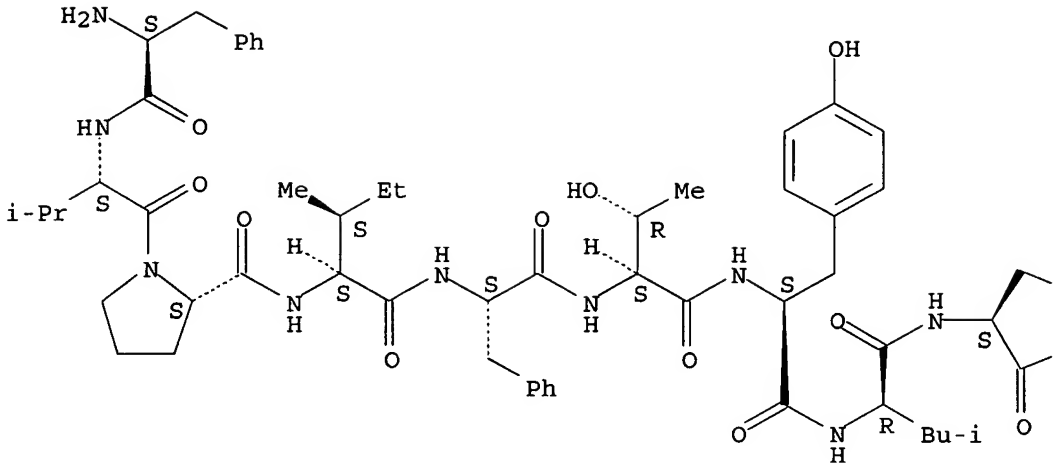
PAGE 2-A



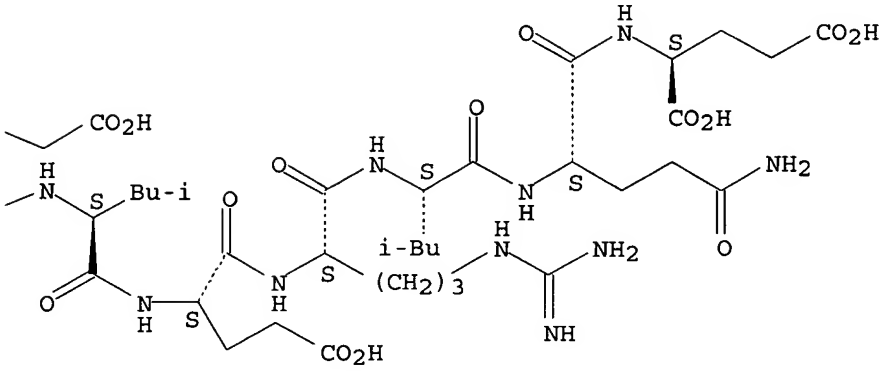
RN 70646-11-6 HCAPLUS
CN Motilin (swine), 8-D-leucine-11-L-glutamic acid-13-L-leucine-16-de-L-lysine-17-de-L-glutamic acid-18-de-L-arginine-19-de-L-asparagine-20-de-L-lysine-21-deglycine-22-de-L-glutamine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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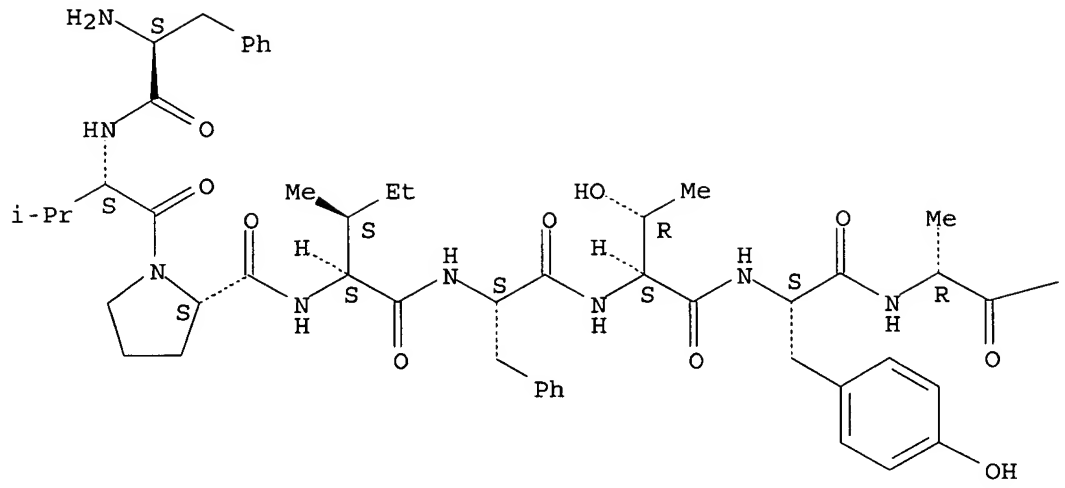
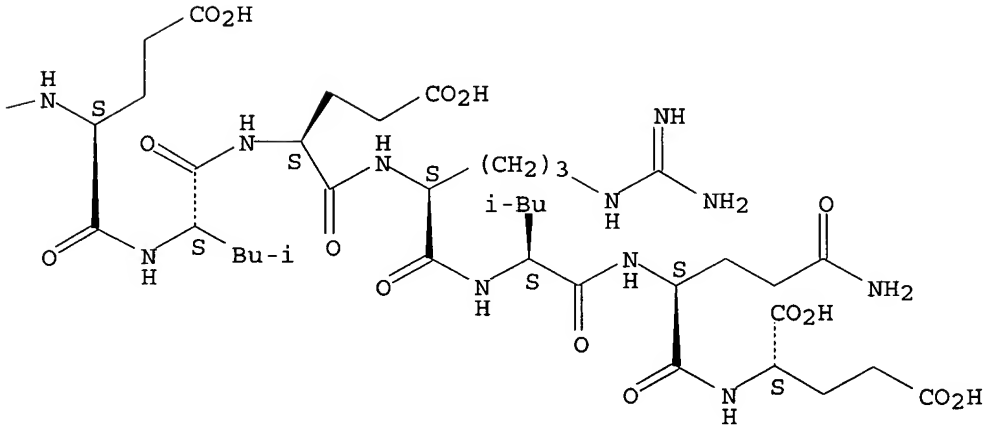
CN Motilin (swine), 8-D-alanine-11-L-glutamic acid-13-L-leucine-16-de-L-lysine-17-de-L-glutamic acid-18-de-L-arginine-19-de-L-asparagine-20-de-L-lysine-21-deglycine-22-de-L-glutamine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



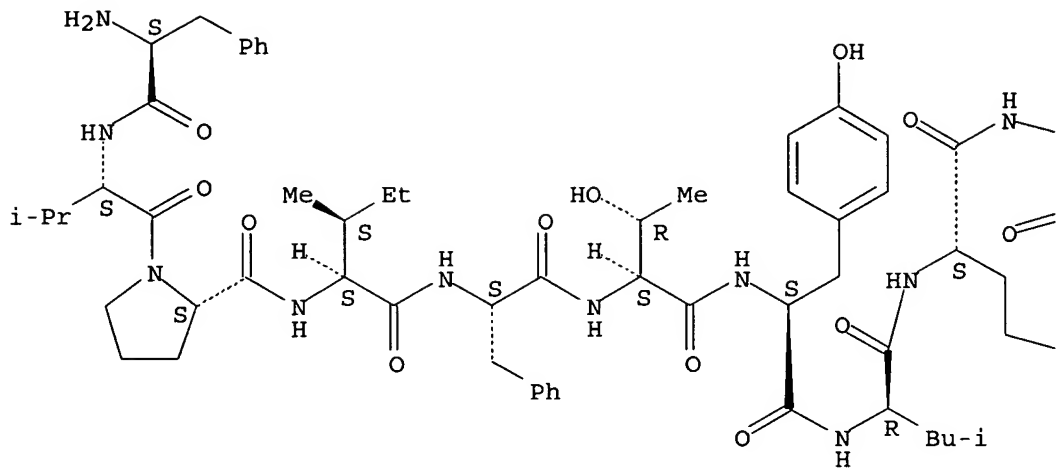
PAGE 1-B



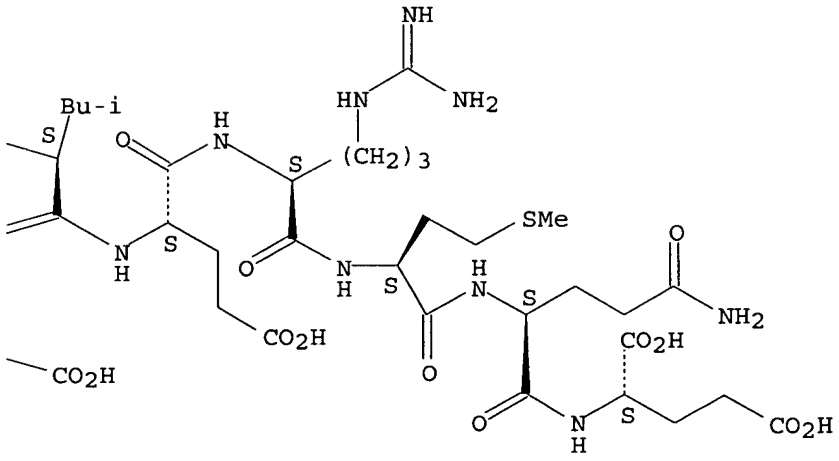
RN 70646-17-2 HCAPLUS
CN Motilin (swine), 8-D-leucine-11-L-glutamic acid-16-de-L-lysine-17-de-L-glutamic acid-18-de-L-arginine-19-de-L-asparagine-20-de-L-lysine-21-deglycine-22-de-L-glutamine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



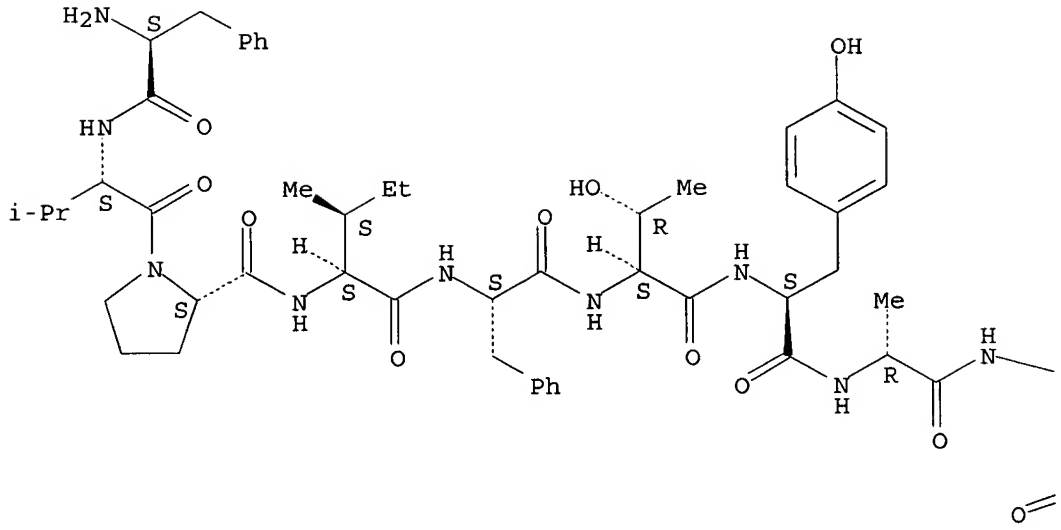
PAGE 1-B



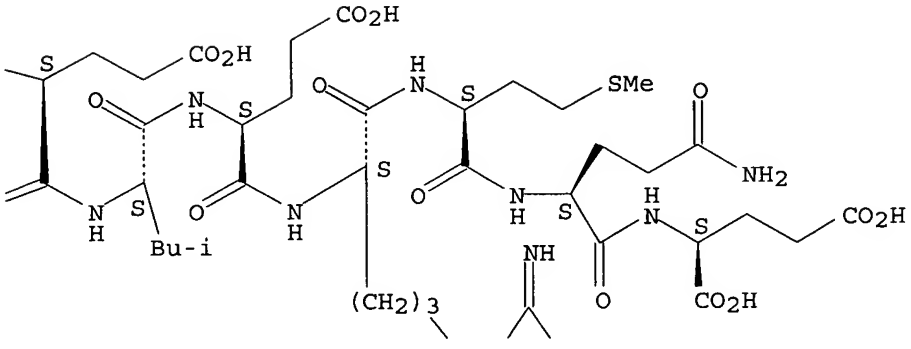
RN 70646-21-8 HCAPLUS
CN Motilin (swine), 8-D-alanine-11-L-glutamic acid-16-de-L-lysine-17-de-L-glutamic acid-18-de-L-arginine-19-de-L-asparagine-20-de-L-lysine-21-deglycine-22-de-L-glutamine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

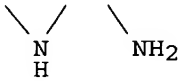
PAGE 1-A



PAGE 1-B



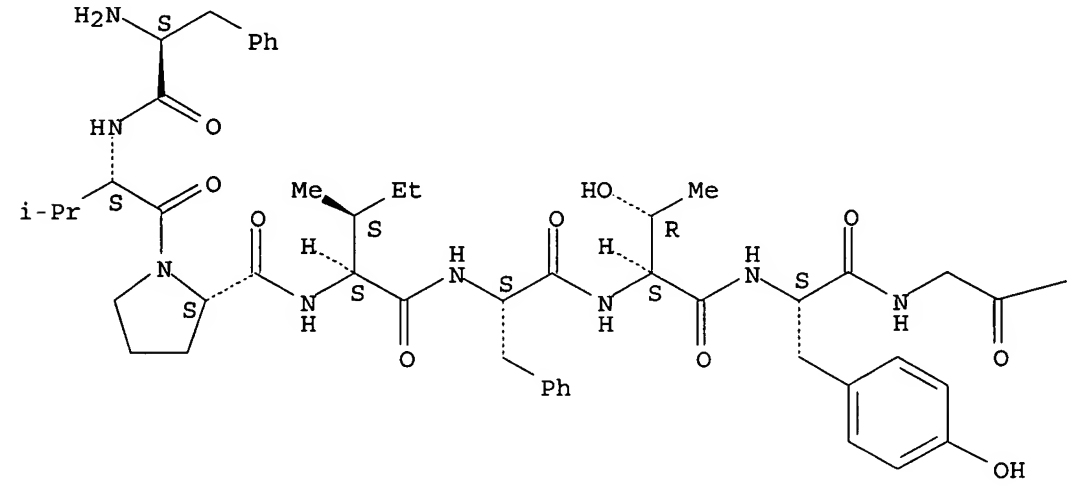
PAGE 2-B



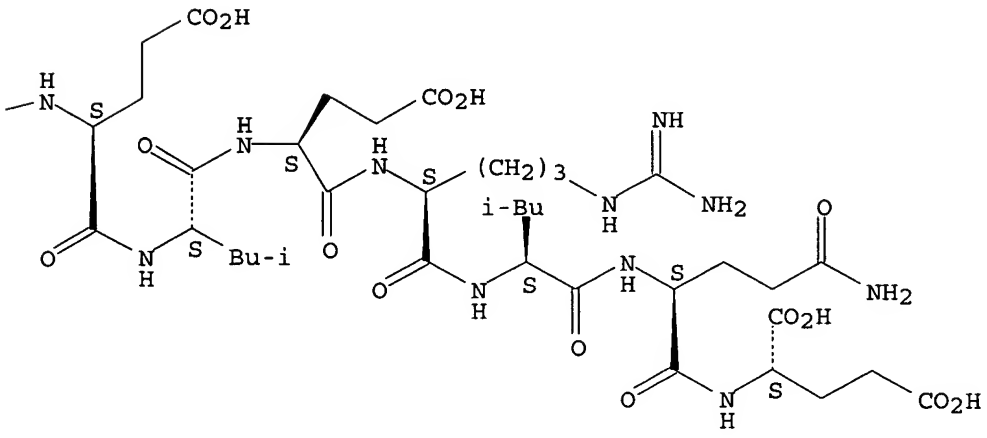
RN 70646-23-0 HCAPLUS
CN Motilin (swine), 11-L-glutamic acid-13-L-leucine-16-de-L-lysine-17-de-L-glutamic acid-18-de-L-arginine-19-de-L-asparagine-20-de-L-lysine-21-deglycine-22-de-L-glutamine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



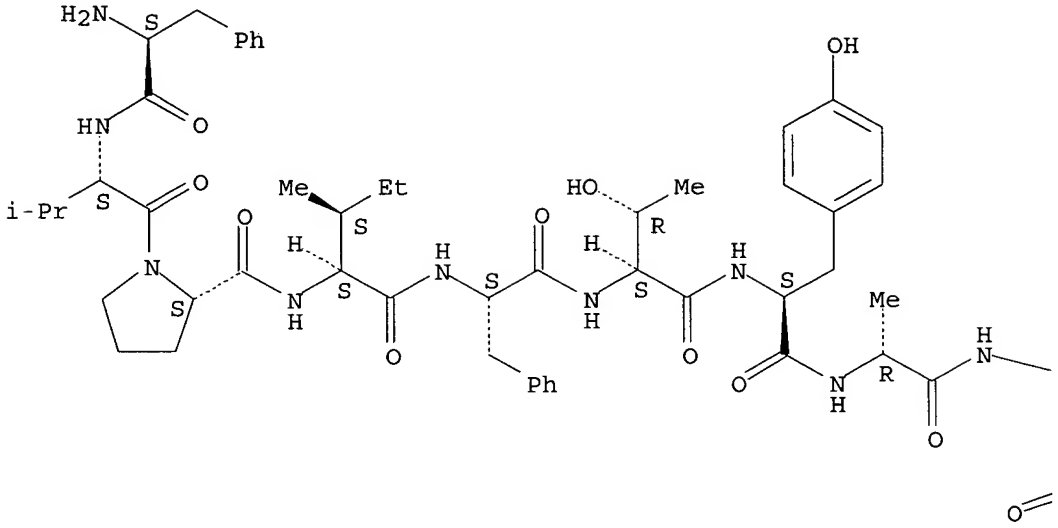
PAGE 1-B



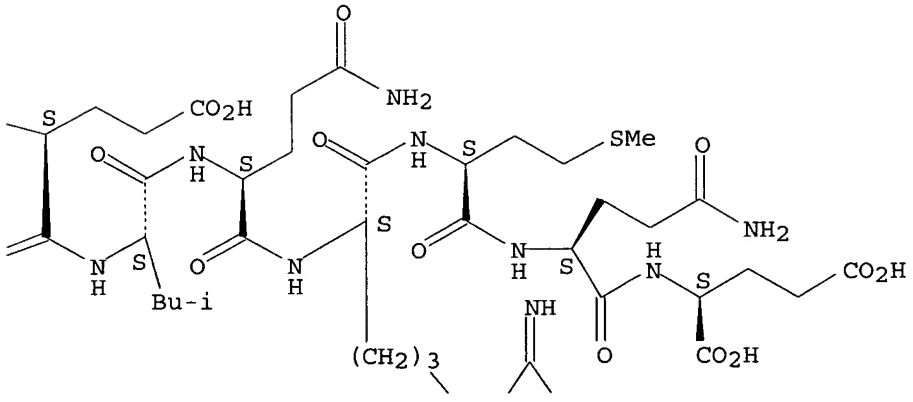
RN 70646-24-1 HCAPLUS
CN Motilin (swine), 8-D-alanine-16-de-L-lysine-17-de-L-glutamic acid-18-de-L-arginine-19-de-L-asparagine-20-de-L-lysine-21-deglycine-22-de-L-glutamine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

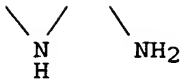
PAGE 1-A



PAGE 1-B



PAGE 2-B



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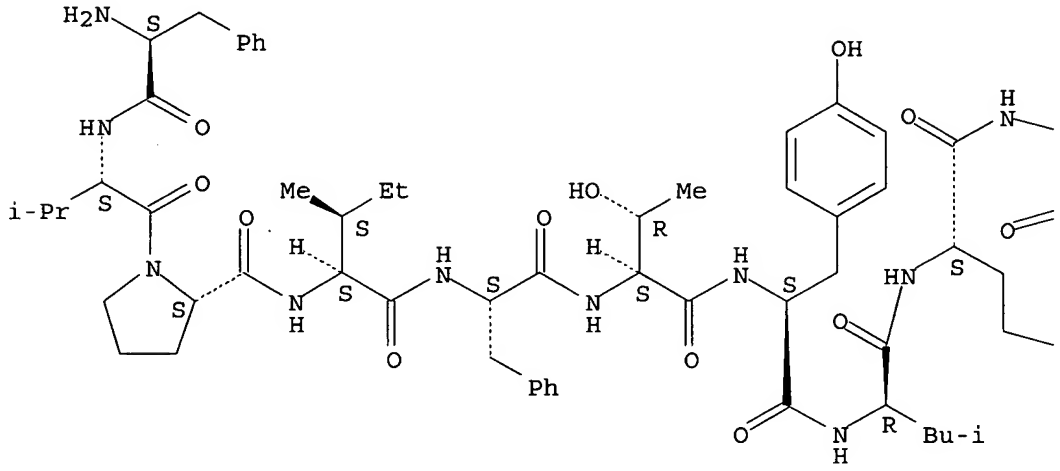
Absolute stereochemistry.

PAGE 1-A



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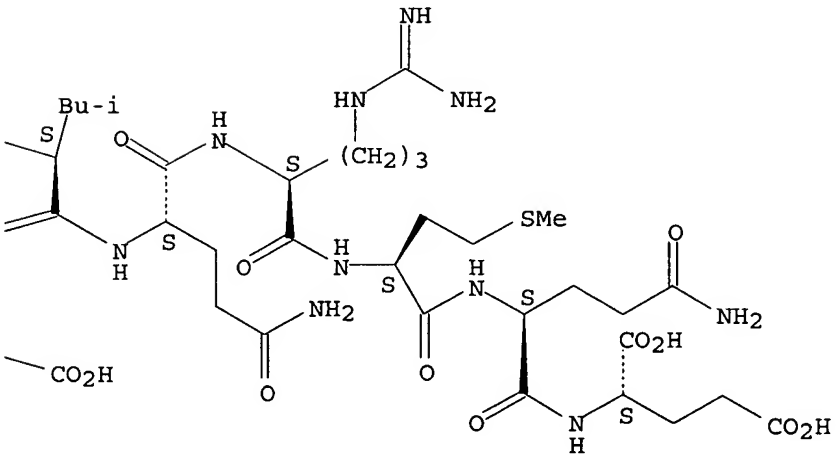


L17 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

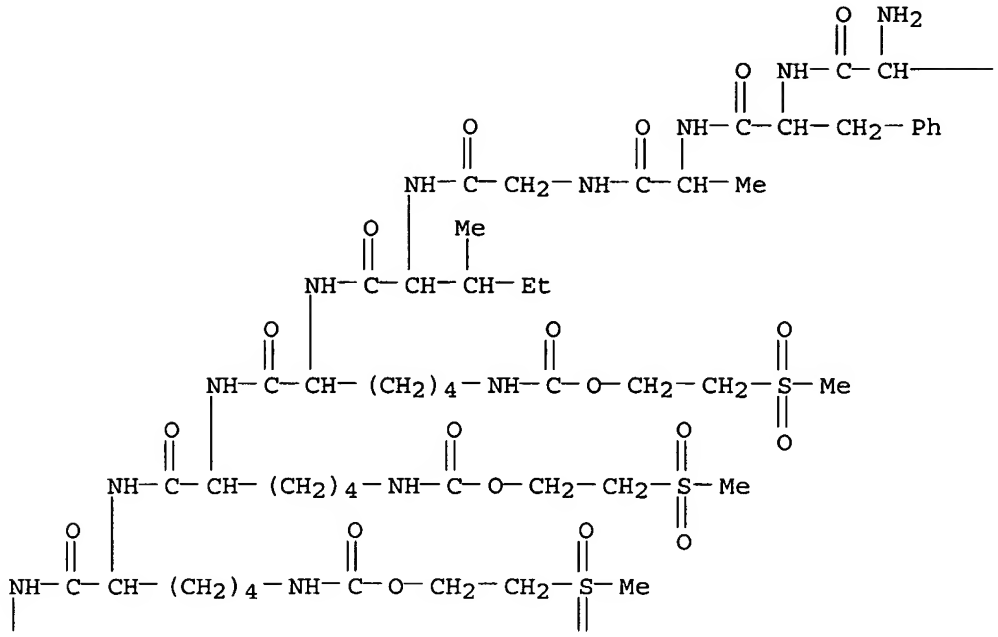
ACCESSION NUMBER: 1979:147219 HCAPLUS
DOCUMENT NUMBER: 90:147219
TITLE: Semisynthetic horse heart [65-homoserine]cytochrome c from three fragments
AUTHOR(S): Boon, Peter J.; Tesser, Godefridus I.; Nivard, Rutger J. F.
CORPORATE SOURCE: Dep. Org. Chem., Cathol. Univ., Nijmegen, Neth.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (**1979**), 76(1), 61-5
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Horse heart cytochrome c was treated with methylsulfonylethyloxycarbonyl succinimide (Msc-ONSu) to give fully Nε-protected cytochrome c. Treatment with this derivative with a hard base for 15 s regenerated the native tetradecapeptide chain. CNBr degradation of the protected compound produced 3 fragments bearing only protective Msc functions on ε-NH2 groups. The fragment comprising the sequence 81-104 was isolated from the mixture and acylated with N-hydroxysuccinimidyl-tert-butyloxycarbonyl-L-methioninate. The resulting pentacosapeptide derivative was partially deprotected by treatment with acid and condensed in good yield (65%) with fully synthetic Nα66,Nε72,73,79-tetra-Msc-cytochrome-c-(66-79)-tetradecapeptide azide. Subsequent treatment of the product with a base produced unprotected semisynthetic cytochrome-c-(66-104)-nonatriacontapeptide, which underwent acylation by unprotected homoserine-65 (Hse65)cytochrome c-(1-65)-pentahexacontapeptide lactone. The high specificity of this **condensation** was ascribed to conformation direction. Semisynthetic [Hse65]cytochrome c thus prepared reacted like native cytochrome c with a succinate cytochrome c **reductase** preparation and with cytochrome c oxidase. This semisynthetic strategy may provide a rapid route for the production of cytochrome c analogs modified in the highly conservative sequence 66-80.

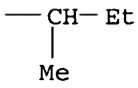
IT **69630-95-1P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling reaction of)

RN 69630-95-1 HCAPLUS
CN L-Glutamic acid, L-isoleucyl-L-phenylalanyl-L-alanylglycyl-L-isoleucyl-N6-[[2-(methylsulfonyl)ethoxy]carbonyl]-L-lysyl-N6-[[2-(methylsulfonyl)ethoxy]carbonyl]-L-lysyl-N6-[[2-(methylsulfonyl)ethoxy]carbonyl]-L-lysyl-L-threonyl-L-α-glutamyl-L-arginyl-L-α-glutamyl-L-α-aspartyl-L-leucyl-L-isoleucyl-L-alanyl-L-tyrosyl-L-leucyl-N6-[[2-(methylsulfonyl)ethoxy]carbonyl]-L-lysyl-N6-[[2-(methylsulfonyl)ethoxy]carbonyl]-L-lysyl-L-alanyl-L-threonyl-L-asparaginyl- (9CI) (CA INDEX NAME)

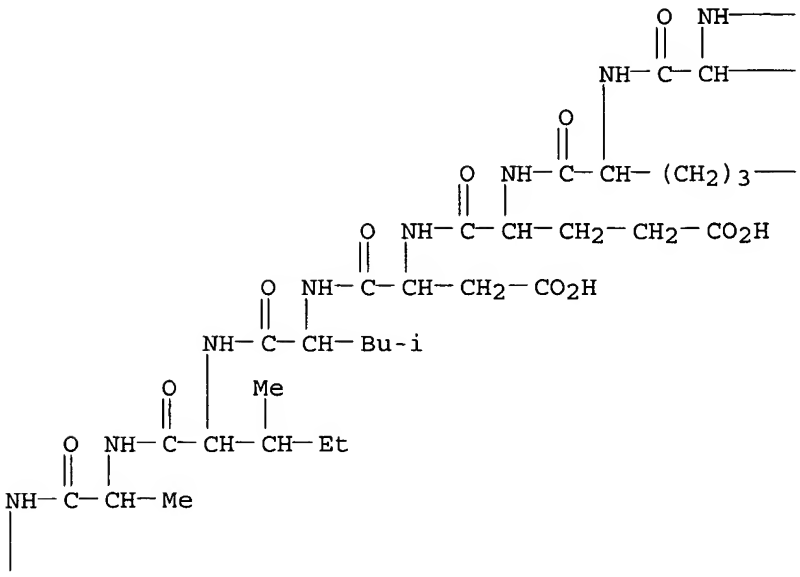
PAGE 1-B



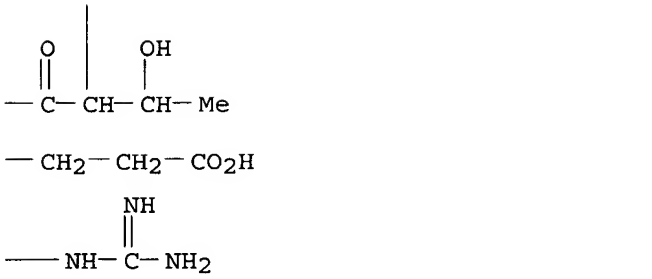
PAGE 1-C



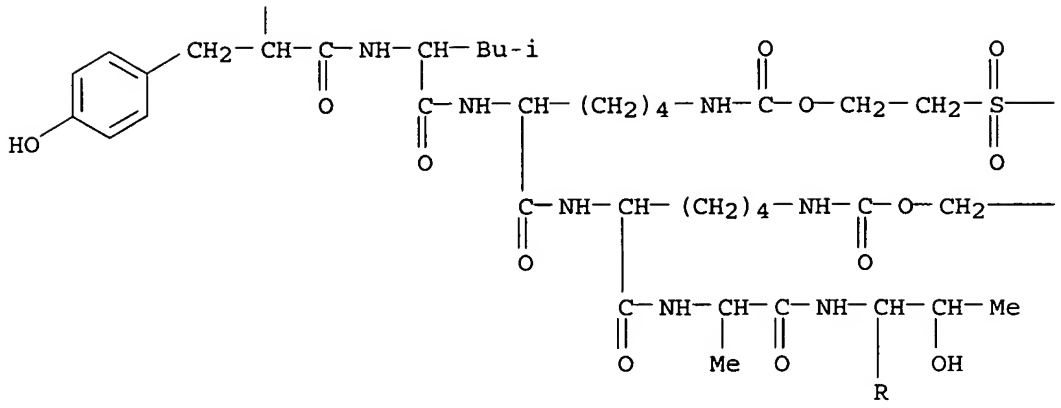
PAGE 2-A



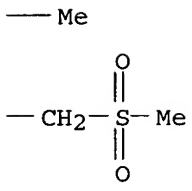
PAGE 2-B



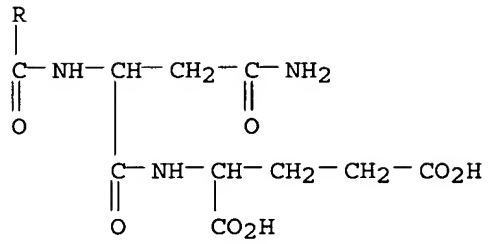
PAGE 3-A



PAGE 3-B



PAGE 4-A



L17 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1978:406537 HCAPLUS
DOCUMENT NUMBER: 89:6537
TITLE: Model polypeptides for α-helix coiled coil proteins. II. Synthesis and characterization of poly(Ala-Leu-Lys-Glu-Ala2-Glu)
AUTHOR(S): Treiber, L. R.; Wong, W. Mai; Shen, M. E.; Walton, A. G.
CORPORATE SOURCE: Dep. Macromol. Sci., Case Western Reserve Univ., Cleveland, OH, USA
SOURCE: International Journal of Peptide & Protein Research (**1977**), 10(5), 349-62

CODEN: IJPPC3; ISSN: 0367-8377
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The title polypeptide (I), which has a repeat sequence of hydrophobic residues in α-keratin and tropomyosin, of mol. weight up to 47,000 was prepared by polymerizing H-Ala-Leu-Lys(CO2CH2Ph)-Glu(OCH2Ph)-Ala-Ala-Glu(OCH2Ph)-OC6H4OH-2 (II) and deblocking with HBr/HOAc. II was prepared by stepwise active ester couplings. I with a d.p. of 25 and a uniform mol. weight of 18,250 was prepared by 25 **condensations** of heptapeptide units. CD data showed that I has a random conformation in aqueous solution at all pH; however high mol. weight I (.apprx.40,000) has 20-30% α-helix in aqueous solution at pH 7 and at 25°. The α-helix content of I could be increased to 50-60% by addition of α-helix-forming solvents. Electron diffraction and x-ray diffraction data showed α-helix coils for I in the solid state.

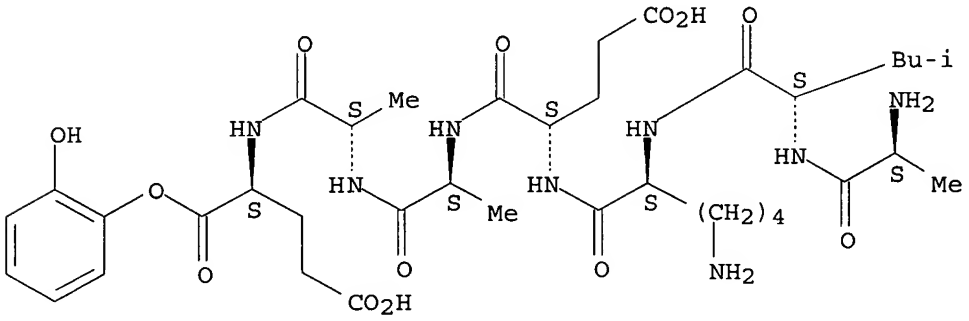
IT **66245-90-7P 66293-15-0P**
RL: PRP (Properties); **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation and conformation of)

RN 66245-90-7 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N-[N2-(N-L-alanyl-L-leucyl)-L-lysyl]-L-α-glutamyl]-L-alanyl]-L-alanyl]-, 1-(2-hydroxyphenyl) ester, homopolymer (9CI) (CA INDEX NAME)

CM 1

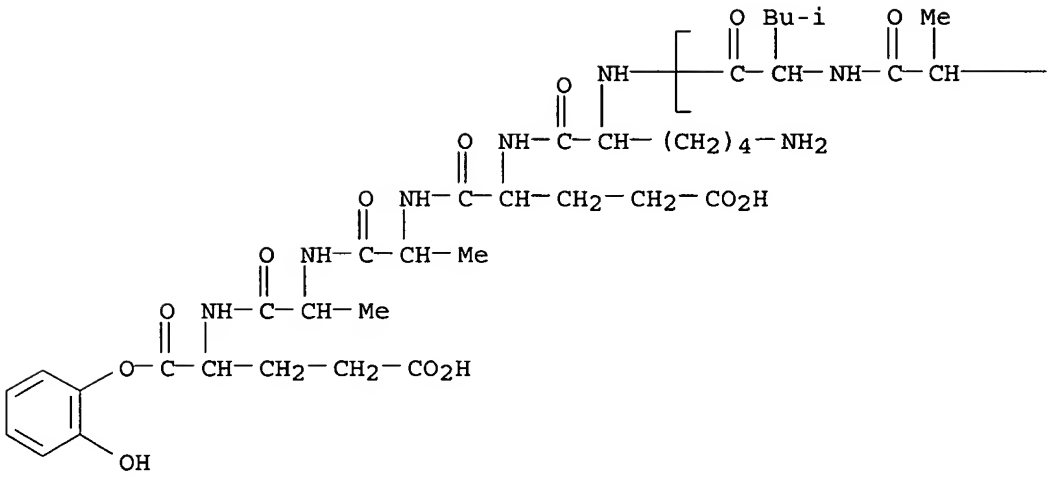
CRN 66245-89-4
CMF C37 H58 N8 O13

Absolute stereochemistry.

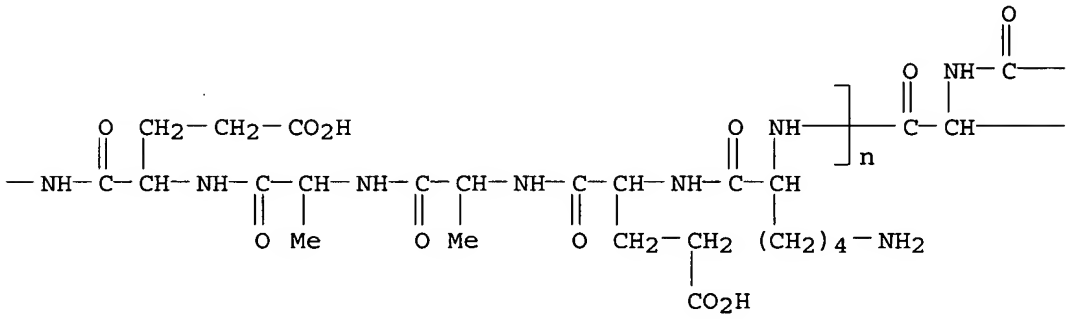


RN 66293-15-0 HCAPLUS
CN Poly[imino[1-(4-aminobutyl)-2-oxo-1,2-ethanediyl]imino[1-(2-carboxyethyl)-2-oxo-1,2-ethanediyl]imino(1-methyl-2-oxo-1,2-ethanediyl)imino(1-methyl-2-oxo-1,2-ethanediyl)imino[1-(2-carboxyethyl)-2-oxo-1,2-ethanediyl]imino(1-methyl-2-oxo-1,2-ethanediyl)imino[1-(2-methylpropyl)-2-oxo-1,2-ethanediyl]], α-[2-[(2-amino-1-oxopropyl)amino]-4-methyl-1-oxopentyl]-ω-[[5-amino-1-[[[3-carboxy-1-[[[2-[[2-[[3-carboxy-1-[(2-hydroxyphenoxy)carbonyl]propyl]amino]-1-methyl-2-oxoethyl]amino]-1-methyl-2-oxoethyl]amino]carbonyl]propyl]amino]carbonyl]pentyl]amino]-, (all-S)- (9CI) (CA INDEX NAME)

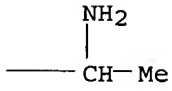
PAGE 1-A



PAGE 1-B



PAGE 1-C



—Bu-i

IT **66245-88-3P 66285-26-5P 66630-69-1P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and deblocking of)
RN 66245-88-3 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N-[N2-(N-L-alanyl-L-leucyl)-N6-[(phenylmethoxy)carbonyl]-L-lysyl]-L-α-glutamyl]-L-alanyl]-L-alanyl]-

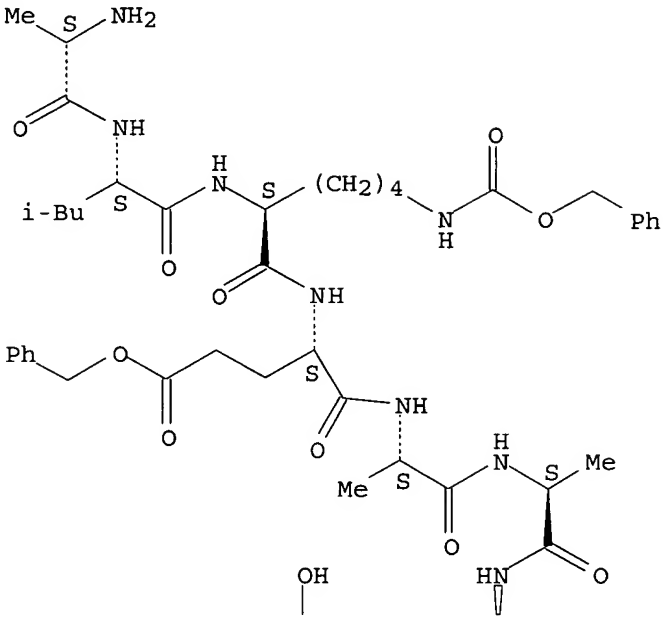
, 1-(2-hydroxyphenyl) 5,5'-bis(phenylmethyl) ester, homopolymer (9CI) (CA INDEX NAME)

CM 1

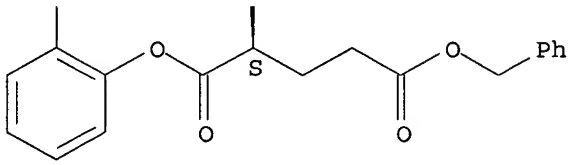
CRN 66245-87-2
CMF C59 H76 N8 O15

Absolute stereochemistry.

PAGE 1-A



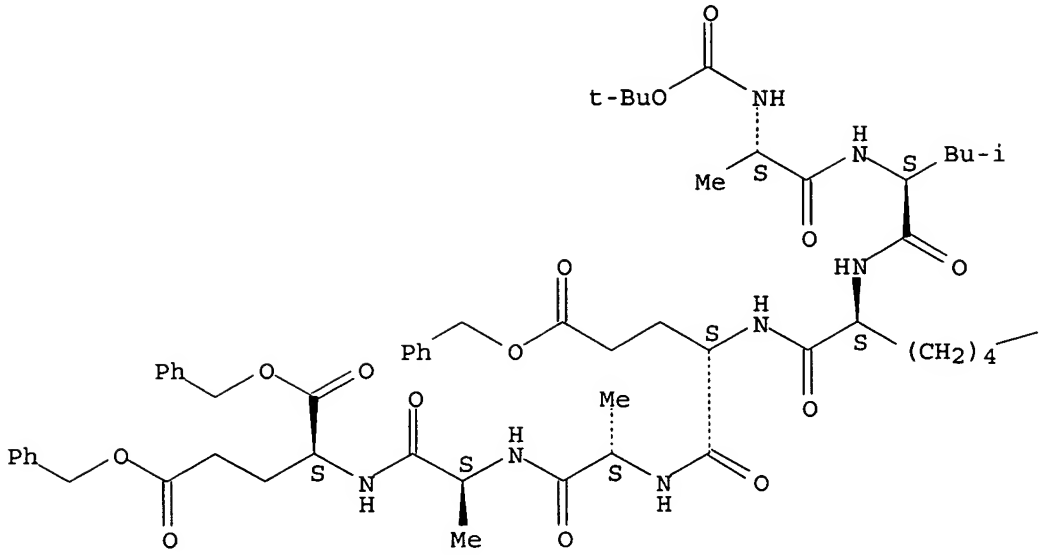
PAGE 2-A



RN 66285-26-5 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N-[N2-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl]-L-leucyl]-N6-[(phenylmethoxy)carbonyl]-L-lysyl]-L-α-glutamyl]-L-alanyl]-L-alanyl]-, tris(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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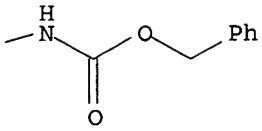
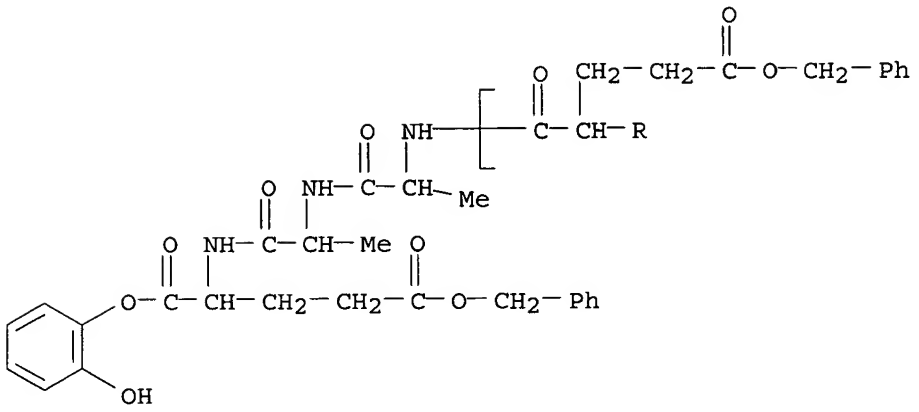


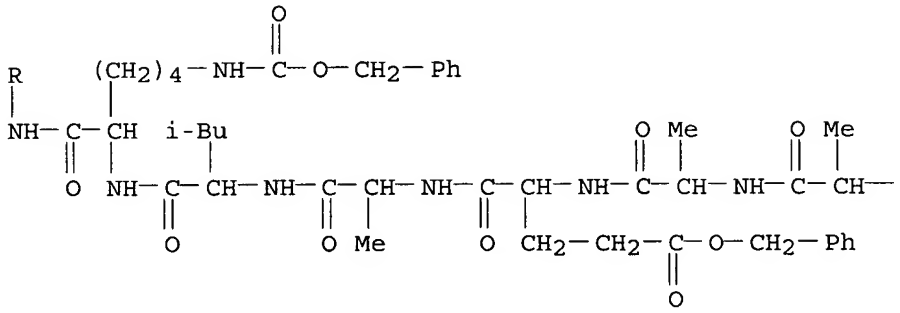
RN 66630-69-1 HCAPLUS

CN Poly[imino(1-methyl-2-oxo-1,2-ethanediyl)imino(1-methyl-2-oxo-1,2-ethanediyl)imino[2-oxo-1-[3-oxo-3-(phenylmethoxy)propyl]-1,2-ethanediyl]imino(1-methyl-2-oxo-1,2-ethanediyl)imino[1-(2-methylpropyl)-2-oxo-1,2-ethanediyl]imino[2-oxo-1-[4-[[(phenylmethoxy)carbonyl]amino]butyl]-1,2-ethanediyl]imino[2-oxo-1-[3-oxo-3-(phenylmethoxy)propyl]-1,2-ethanediyl]], α-[N-[N2-(N-L-alanyl-L-leucyl)-N6-[(phenylmethoxy)carbonyl]-L-lysyl]-L-α-glutamyl]-ω-[[2-[[2-[[1-[(2-hydroxyphenoxy)carbonyl]-4-oxo-4-(phenylmethoxy)butyl]amino]-1-methyl-2-oxoethyl]amino]-1-methyl-2-oxoethyl]amino]-, phenylmethyl ester, (all-S)- (9CI) (CA INDEX NAME)

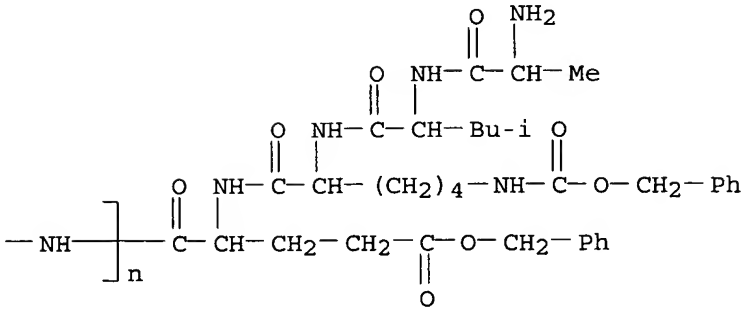
PAGE 1-A



PAGE 2-A



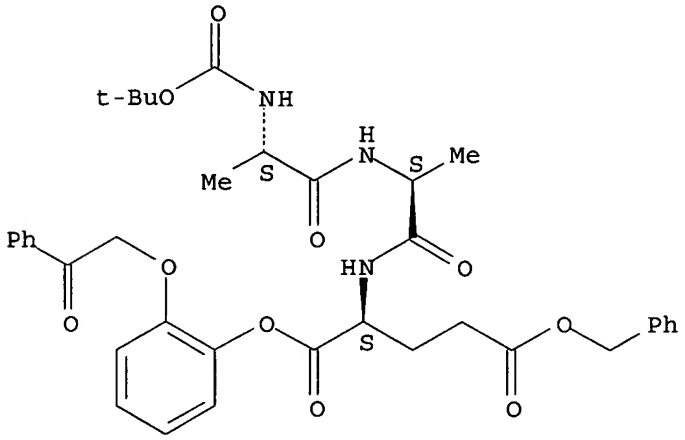
PAGE 2-B



IT **66285-15-2P 66285-17-4P 66285-19-6P**
66285-21-0P 66285-24-3P 66285-29-8P
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation and partial deblocking of)
RN 66285-15-2 HCAPLUS

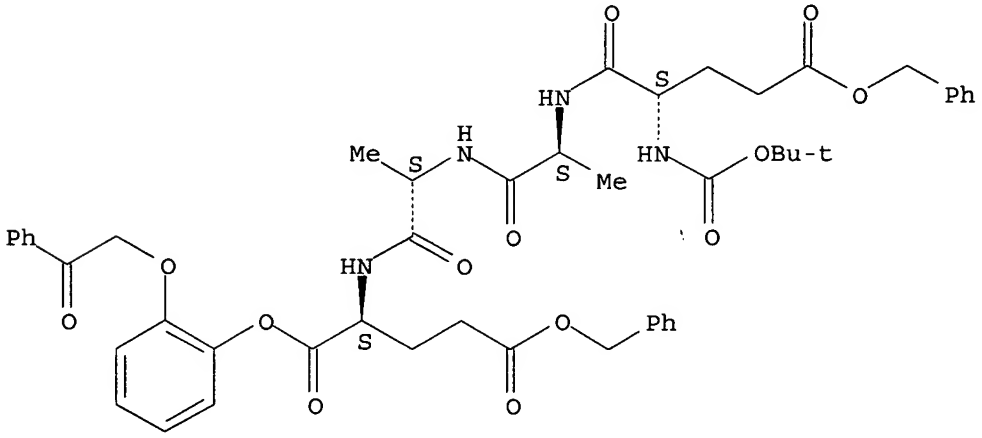
CN L-Glutamic acid, N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl]-L-alanyl]-, 1-[2-(2-oxo-2-phenylethoxy)phenyl] 5-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 66285-17-4 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-α-glutamyl]-L-alanyl]-L-alanyl]-, 1-[2-(2-oxo-2-phenylethoxy)phenyl] 5,5'-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

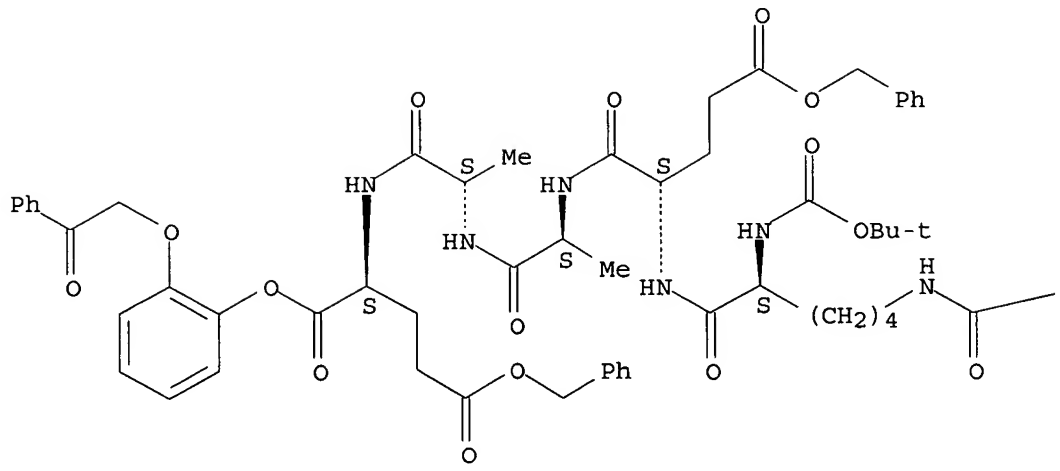
Absolute stereochemistry.



RN 66285-19-6 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N-[N2-[(1,1-dimethylethoxy)carbonyl]-N6-[(phenylmethoxy)carbonyl]-L-lysyl]-L-α-glutamyl]-L-alanyl]-L-alanyl]-, 1-[2-(2-oxo-2-phenylethoxy)phenyl] 5,5'-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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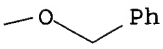
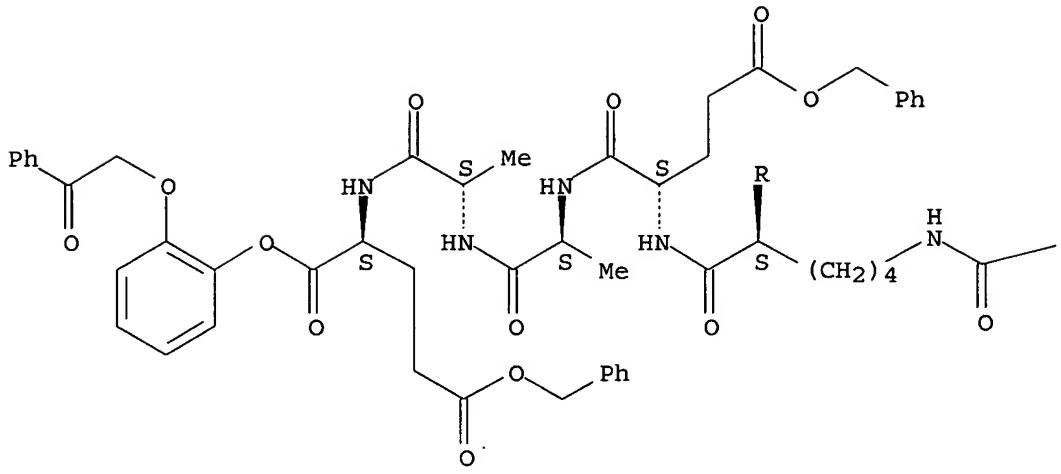


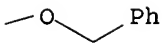
RN 66285-21-0 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N-[N2-[N-[(1,1-dimethylethoxy)carbonyl]-L-leucyl]-N6-[(phenylmethoxy)carbonyl]-L-lysyl]-L-α-glutamyl]-L-alanyl]-L-alanyl]-, 1-[2-(2-oxo-2-phenylethoxy)phenyl] 5,5'-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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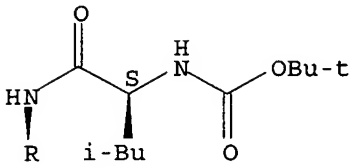
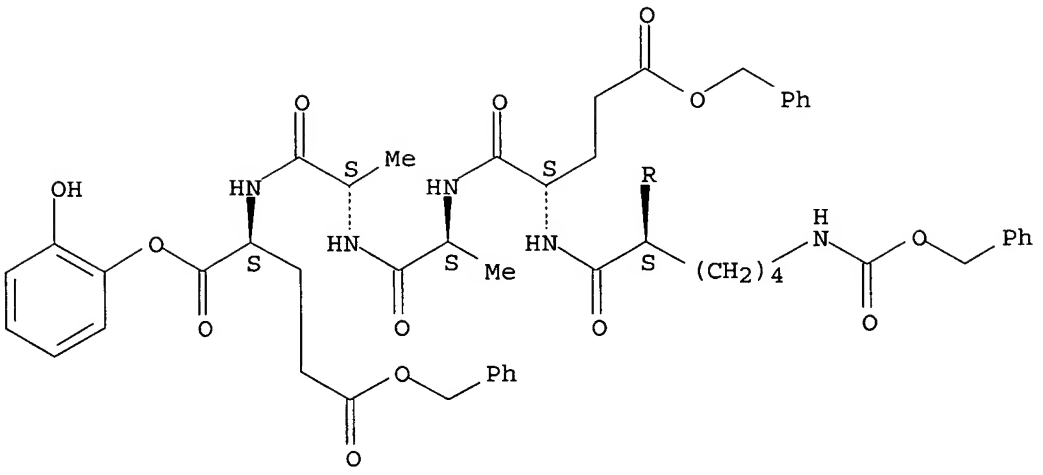


RN 66285-24-3 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N-[N2-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl]-L-leucyl]-N6-[(phenylmethoxy)carbonyl]-L-lysyl]-L-α-glutamyl]-L-alanyl]-L-alanyl]-, 1-(2-hydroxyphenyl) 5,5'-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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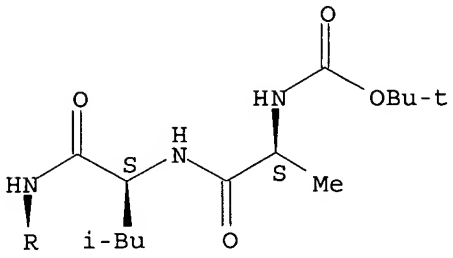
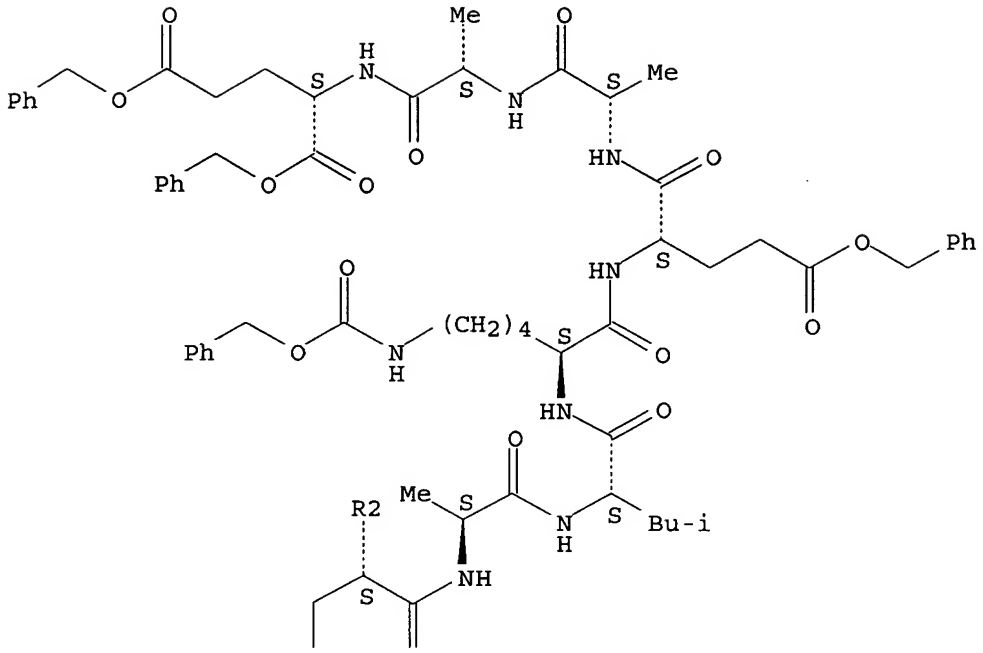


RN 66285-29-8 HCAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl-L-leucyl-N6-[(phenylmethoxy)carbonyl]-L-lysyl-L-α-glutamyl-L-alanyl-L-alanyl-L-α-glutamyl-L-alanyl-L-leucyl-N6-[(phenylmethoxy)carbonyl]-L-lysyl-L-α-glutamyl-L-alanyl-L-alanyl-, pentakis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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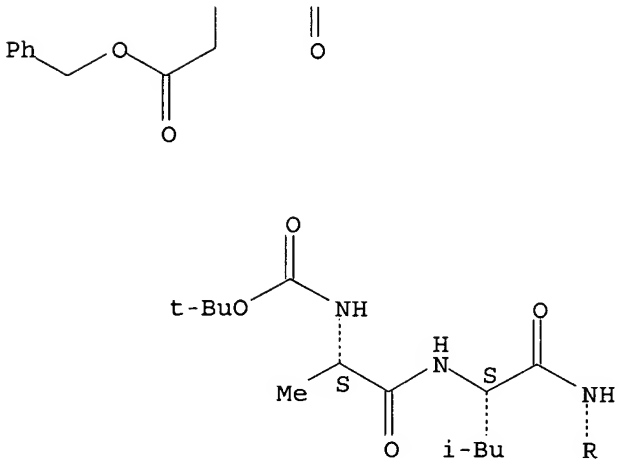

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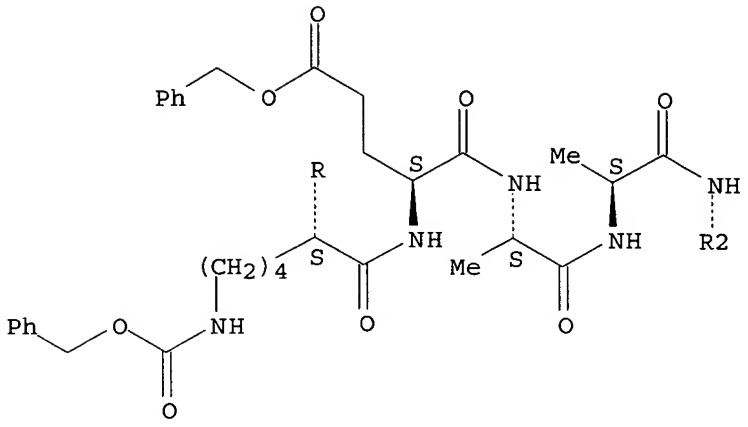


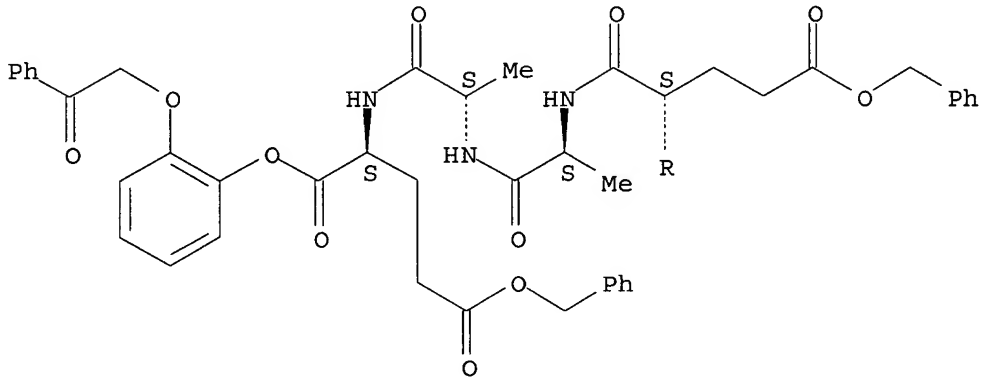
IT **66285-22-1P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with alanine derivative)

RN 66285-22-1 HCAPLUS

CN L-Glutamic acid, N-[N-[N-[N-[N2-L-leucyl-N6-[(phenylmethoxy)carbonyl]-L-lysyl]-L-α-glutamyl]-L-alanyl]-L-alanyl]-, 1-[2-(2-oxo-2-phenylethoxy)phenyl] 5,5'-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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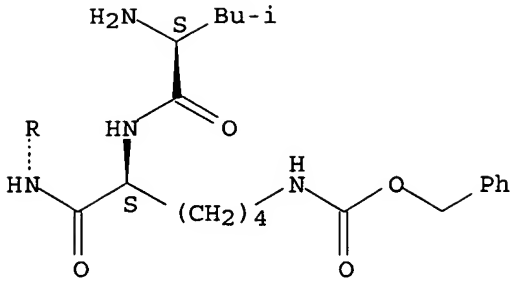
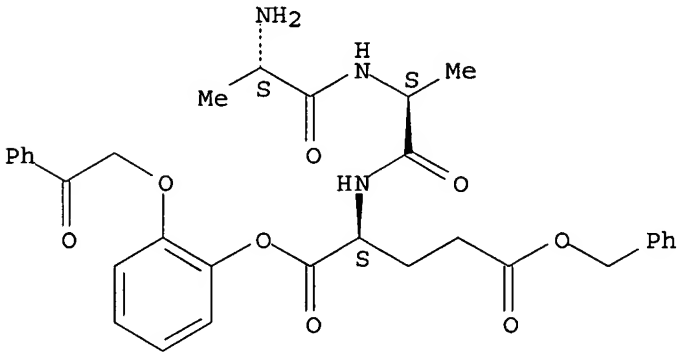


IT **66285-16-3P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with glutamic acid derivative)
RN 66285-16-3 HCAPLUS
CN L-Glutamic acid, N-(N-L-alanyl-L-alanyl)-, 1-[2-(2-oxo-2-phenylethoxy)phenyl] 5-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



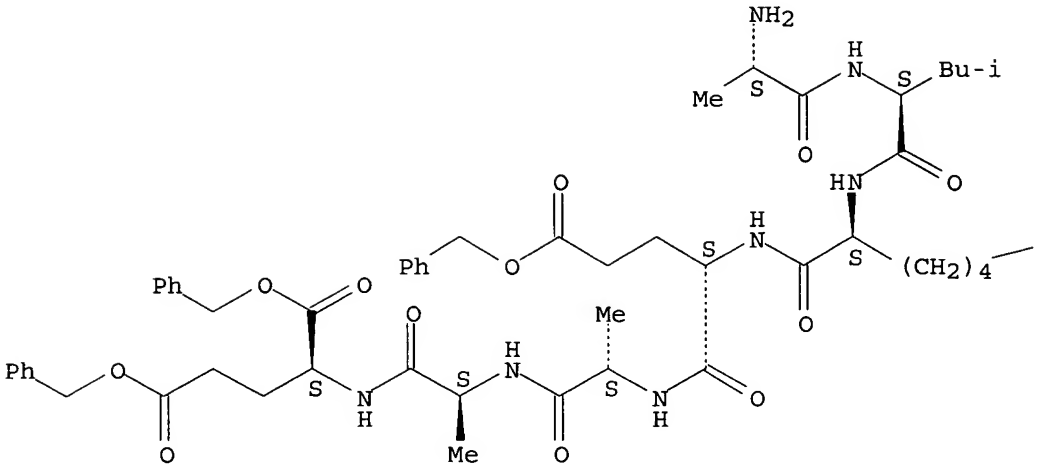
IT **66285-28-7P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with heptapeptide derivative)
RN 66285-28-7 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N-[N2-(N-L-alanyl-L-leucyl)-N6-[(phenylmethoxy)carbonyl]-L-lysyl]-L-α-glutamyl]-L-alanyl]-L-alanyl]-, tris(phenylmethyl) ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 66285-27-6
CMF C60 H78 N8 O14

Absolute stereochemistry.

PAGE 1-A



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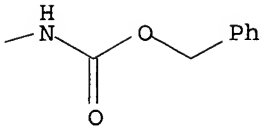
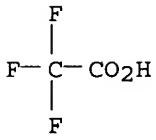


CM 2

CRN 76-05-1
CMF C2 H F3 O2

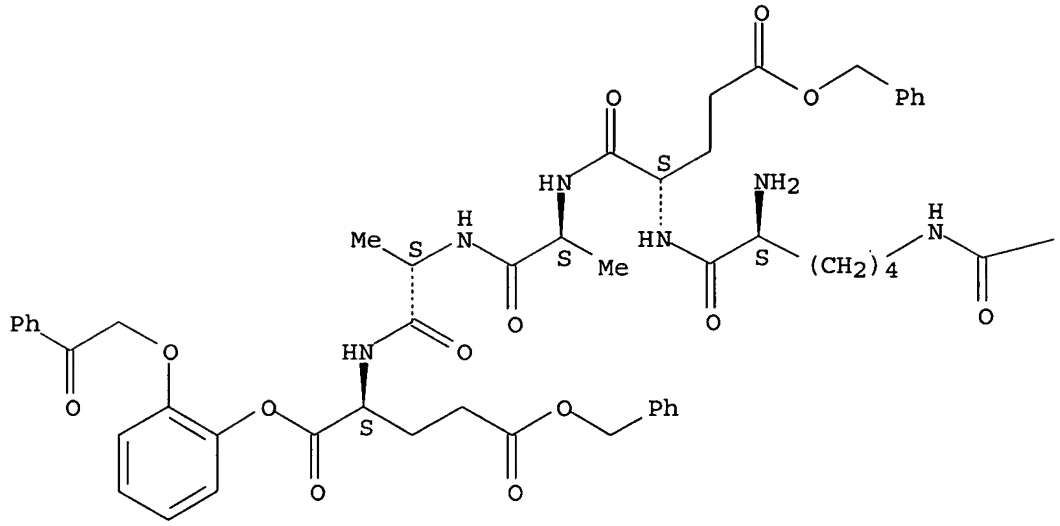


IT **66285-20-9P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with leucine derivative)
RN 66285-20-9 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N-[N6-[(phenylmethoxy)carbonyl]-L-lysyl]-L-α-glutamyl]-L-alanyl]-L-alanyl]-, 1-[2-(2-oxo-2-phenylethoxy)phenyl]

5,5'-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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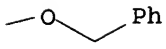
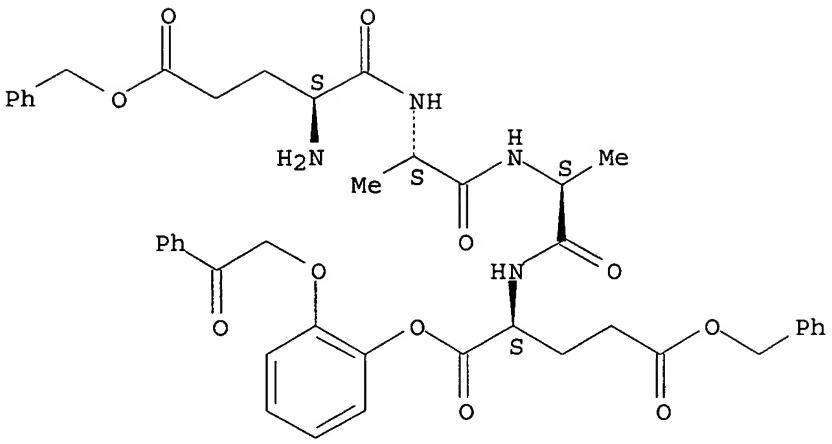


IT **66285-18-5P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with lysine derivative)
RN 66285-18-5 HCAPLUS
CN L-Glutamic acid, N-[N-(N-L-α-glutamyl-L-alanyl)-L-alanyl]-, 1-[2-(2-oxo-2-phenylethoxy)phenyl] 5,5'-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



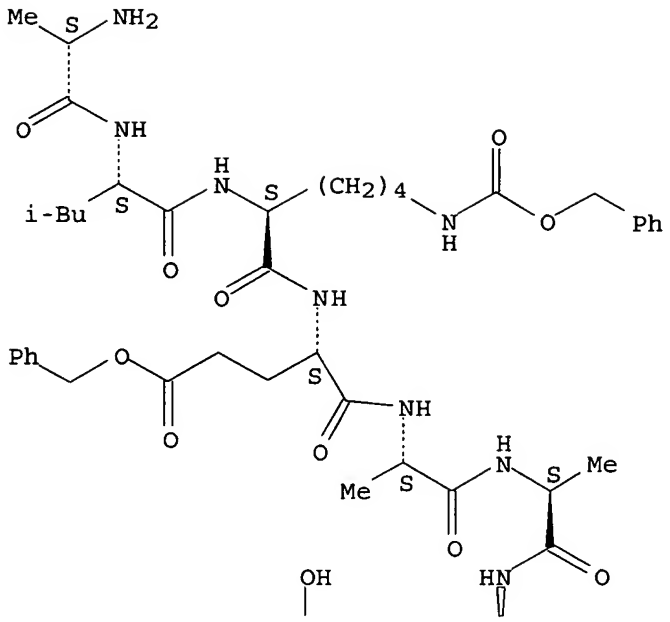
IT **66285-25-4P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; PREP (Preparation); RACT (Reactant or reagent)
(preparation and polymerization of)
RN 66285-25-4 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N-[N2-(N-L-alanyl-L-leucyl)-N6-[(phenylmethoxy)carbonyl]-L-lysyl]-L-α-glutamyl]-L-alanyl]-L-alanyl]-, 1-(2-hydroxyphenyl) 5,5'-bis(phenylmethyl) ester, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 66245-87-2
CMF C59 H76 N8 O15

Absolute stereochemistry.

PAGE 1-A



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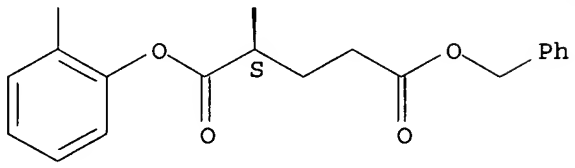
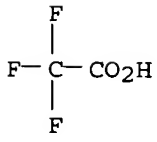


CM 2

CRN 76-05-1
CMF C2 H F3 O2

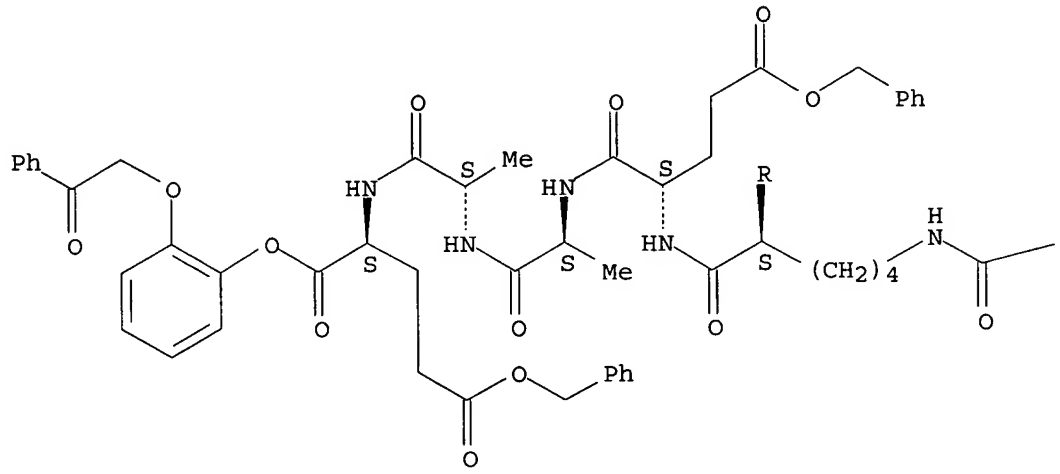


IT **66285-23-2P**
RL: **SPN (Synthetic preparation)**; PREP (Preparation)
(preparation and **reductive** cleavage of phenacyl group of)
RN 66285-23-2 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N-[N2-[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl]-L-leucyl]-N6-[(phenylmethoxy)carbonyl]-L-lysyl]-L-α-

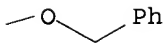
glutamyl]-L-alanyl]-L-alanyl]-, 1-[2-(2-oxo-2-phenylethoxy)phenyl] 5,5'-bis(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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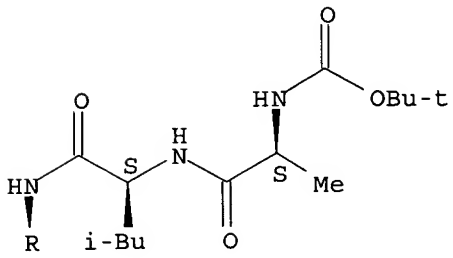

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L3 STR

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=> d ibib abs hitstr l23 1-76

L23  ANSWER 1 OF 76  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:182920  HCAPLUS
DOCUMENT NUMBER:          142:258503
TITLE:                    Secreted polypeptide species in human plasma,
                          detection assays for smaller proteins and tryptic
                          peptides, and expression profiles useful for disease
                          diagnosis
INVENTOR(S):              Argoud-puy, Guilaine; Bederr, Nassima; Bougueleret,
                          Lydie; Cusin, Isabelle; Mahe, Eve; Niknejad, Anne;
                          Reffas, Samia; Rose, Keith; Saudrais,
                          Cedric; Scherer, Andreas; Papoian, Ruben; Dengler, Uwe
                          Jochen; Croft, Laurence James
PATENT ASSIGNEE(S):       Genova Ltd., Bermuda; Novartis Ag; Novartis Pharma
                          GmbH
SOURCE:                   PCT Int. Appl., 284 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2005019825         A2    20050303    WO 2004-EP9323          20040819
     WO 2005019825         A3    20050811
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
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SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-496966P P 20030820

AB The invention relates to polypeptide species secreted in human plasma, isolated polynucleotides encoding such polypeptides, polymorphic variants thereof, and the use of said nucleic acids and polypeptides or compns. thereof for detection assays and disease diagnosis. An industrial-scale method, involving sample pooling, is detailed for the anal. of smaller proteins (mol. weight less than about 40 kDa and mostly under 20 kDa),a nd thousands of peptides resulting from polypeptides can be identified from a single pool. Low abundance proteins such as leptin and ghrelin and peptides such as bradykinin, were clearly identified. By identifying the actual plasma polypeptide species, differences in mRNA processing and splicing, translation rate, mRNA stability, and posttranslational modifications are revealed, and plasma localization points to a novel, previously unknown function for the polypeptides of the invention. Peptides corresponding to 3 specific human plasma polypeptides (HPP) were identified and selected for functional characterization: esophageal cancer-related gene 2 (ECRG2), thymosin β4, and pancreastatin. Treatment of mice with these three HPP species resulted in gene expression profiles showing that these proteins would be useful in diagnosis treatment of cancer or hyperplasia-associated conditions, neurodegeneration or ion balance-associated diseases, and diseases associated with dysregulated serum glucose (e.g., diabetes) or metabolic disorders (e.g., amyloidosis).

IT **845823-78-1 845823-97-4 845825-17-4**

RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

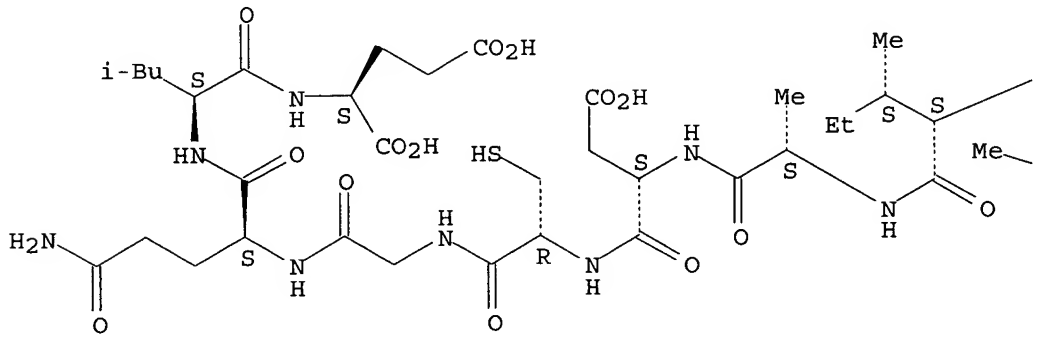
(secreted polypeptide species in human plasma, detection assays for smaller proteins and tryptic peptides, and expression profiles useful for disease diagnosis)

RN 845823-78-1 HCAPLUS

CN L-Glutamic acid, L-lysyl-L-isoleucyl-L-threonyl-L-isoleucyl-L-alanyl-L-α-aspartyl-L-cysteinylglycyl-L-glutaminyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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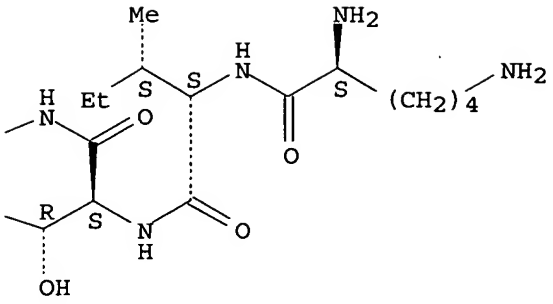
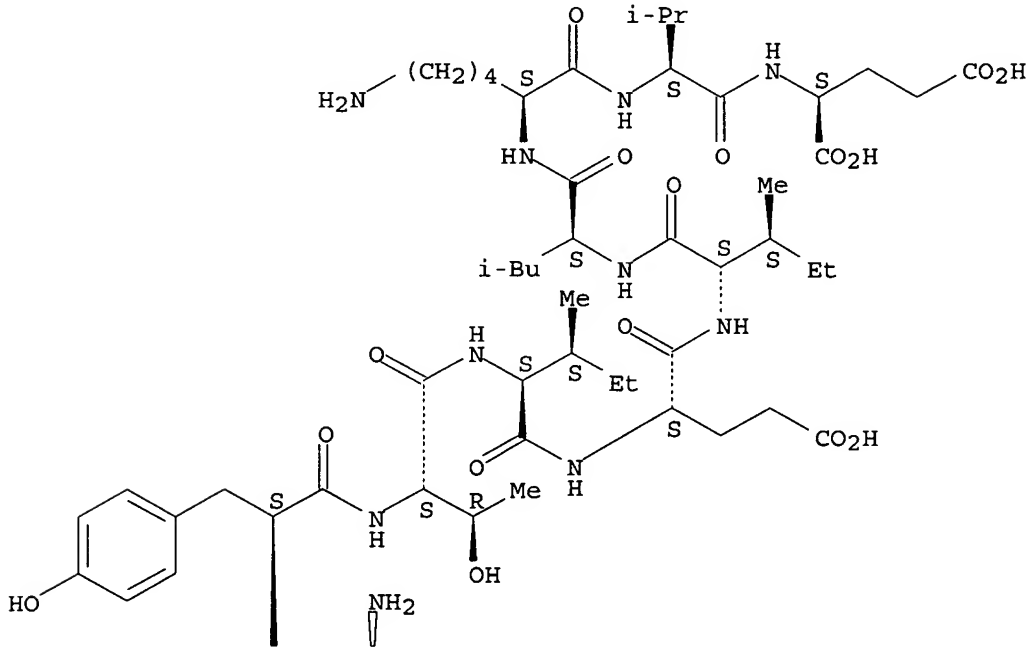


RN 845823-97-4 HCAPLUS
CN L-Glutamic acid, L-phenylalanyl-L-tyrosyl-L-threonyl-L-isoleucyl-L-α-glutamyl-L-isoleucyl-L-leucyl-L-lysyl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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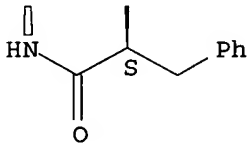
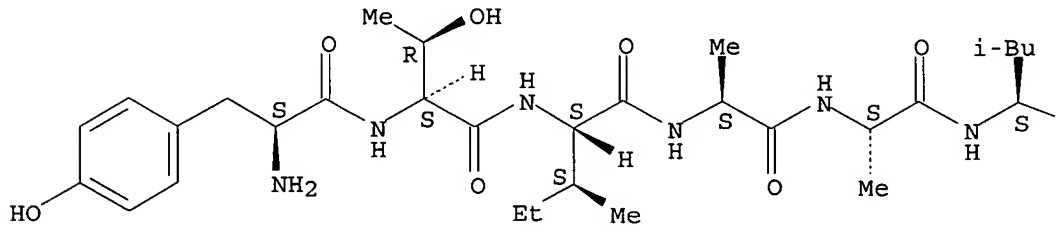


RN 845825-17-4 HCAPLUS

CN L-Glutamic acid, L-tyrosyl-L-threonyl-L-isoleucyl-L-alanyl-L-alanyl-L-leucyl-L-leucyl-L-seryl-L-prolyl-L-tyrosyl-L-seryl-L-tyrosyl-L-seryl-L-threonyl-L-threonyl-L-alanyl-L-valyl-L-valyl-L-threonyl-L-asparaginyl-L-prolyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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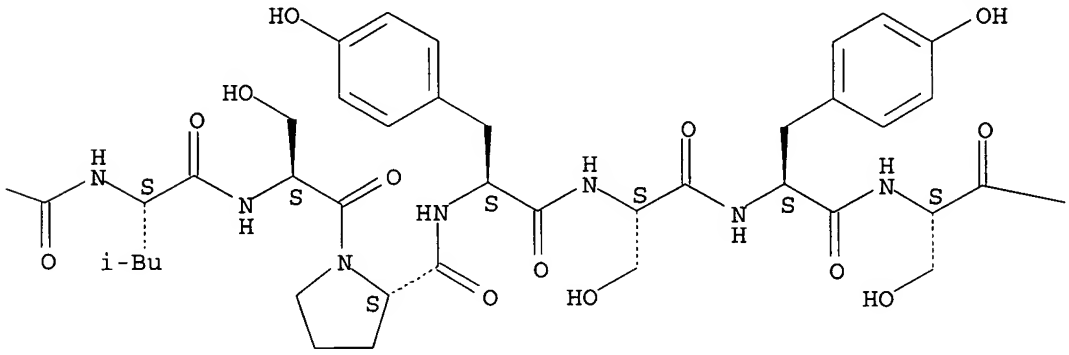

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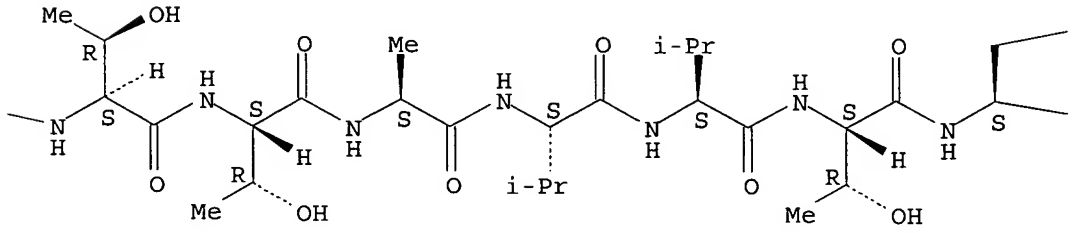
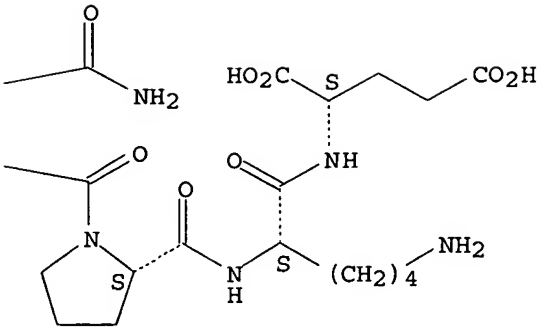




L23 ANSWER 2 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:141350 HCAPLUS
DOCUMENT NUMBER: 142:216622
TITLE: Secreted polypeptide species reduced in cardiovascular disorders, and motilin expression related to intestinal motility disorders
INVENTOR(S): Argoud-Puy, Guilaine; Bederr, Nassima; Bougueleret, Lydie; Cusin, Isabelle; Mahe, Eva; Niknejad, Anne; Reffas, Samia; **Rose, Keith**; Saudrais, Cedric; Scherer, Andreas; Papoian, Ruben
PATENT ASSIGNEE(S): Genova Ltd., Bermuda; Novartis A.-G.; Novartis Pharma G.m.b.H.
SOURCE: 349 pp.
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005015206	A2	20050217	WO 2004-EP8860	20040806
WO 2005015206	A3	20050609		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1654545	A2	20060510	EP 2004-763890	20040806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.:

US 2003-493599P	P	20030808
US 2003-493836P	P	20030808
US 2003-493867P	P	20030808
US 2003-493985P	P	20030808
WO 2004-EP8860	W	20040806

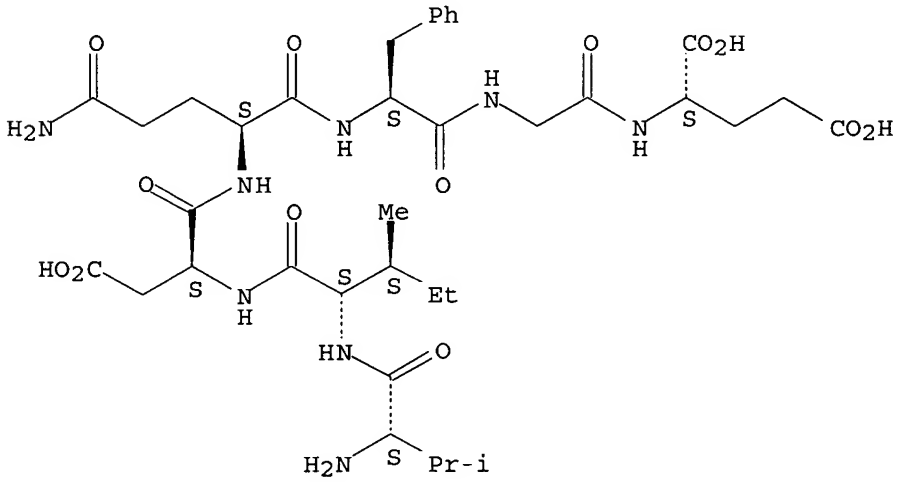
AB The invention discloses human secreted polypeptides that circulate at a decreased level in the plasma of patients with cardiovascular disorders. Thus, 254 Cardiovascular disorder Plasma Polypeptides (CPP 149-402) are identified, by reverse-phase HPLC and mass spectrometry of tryptic peptides, that are differentially reduced in concentration in plasma from individuals with coronary artery disease compared to control plasma. Over-expression of CPP 232, identified as motilin (SwissProt accession number P12872), is also shown to affect the expression of a number of genes/proteins related to intestinal motility, apoptosis pathway, proteosome and ubiquitin pathways, and rRNAs and proteins. Thus, expression of CPP 232 or the genes it regulated may be used for treatment, diagnosis, and monitoring of biliary cirrhosis, gallstones, celiac disease, and other intestinal motility disorders. The invention also provides methods of using compns. including the polypeptides, polynucleotides encoding them, and antibodies specific for these polypeptides, for diagnosis, prognosis, and for drug development.

IT **842158-78-5**
RL: ANT (Analyte); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(tryptic peptide; secreted polypeptide species reduced in cardiovascular disorders, and motilin expression related to intestinal motility disorders)

RN 842158-78-5 HCAPLUS

CN L-Glutamic acid, L-valyl-L-isoleucyl-L-α-aspartyl-L-glutaminyl-L-phenylalanylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 3 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:509551 HCAPLUS

DOCUMENT NUMBER: 140:146468

TITLE: Minimizing the pharmacophore of a potent HIV-1 inhibitor

AUTHOR(S): Devin-Chaloin, Chantal; Moery, Lionel; Hartley, Oliver; **Rose, Keith; Offord, Robin**

CORPORATE SOURCE: Departement de Biochimie Medicale CMU, Geneva, Switz.

SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 389-390. Editor(s):

Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr.
CODEN: 69EDWK; ISBN: 2-84254-048-4
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report. Truncated analogs of NNY-RANTES, containing a PEG-succinimide linker with good activity in HIV fusion assay were synthesized. The PEG-succinimide motif imitated the spatial location of the region replaced by the polyamide. These truncated analogs are useful in identifying the physico-chemical properties and the spatial location of the regions of n-nonanoyl RANTES that are responsible for its activity.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 4 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:295426 HCAPLUS
DOCUMENT NUMBER: 138:319382
TITLE: A Novel Method for the Rational Construction of Well-Defined Immunogens: The Use of Oximation To Conjugate Cholera Toxin B Subunit to a Peptide-Polyoxime Complex
AUTHOR(S): Chen, Jianhua; Zeng, Weiguang; **Offord, Robin**; **Rose, Keith**
CORPORATE SOURCE: Department of Medical Biochemistry, University Medical Center, Geneva, 1211, Switz.
SOURCE: Bioconjugate Chemistry (2003), 14(3), 614-618
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cholera toxin B subunit (CTB), capable of binding to all mucous membranes in its pentameric form, is a potential carrier of mucosal vaccines. In the authors' previous work the authors reported that the N-terminus of CTB, a threonine, could in principle undergo oxidation and oximation to form conjugates with a cascade of immunogenic peptides. In this study, the authors set up a model by chemical coupling CTB to a polyoxime that possessed five copies of influenza virus-derived peptides displayed in comblike form. The construct was reconstituted into pentameric form when eluted from a Superdex column after conjugation, and the pentameric nature of this CTB-viral peptide complex was confirmed by SDS-PAGE. GM1-ELISA assay showed that the binding properties of CTB-viral peptide complex were increased 4-5-fold over native CTB.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 5 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:45103 HCAPLUS
DOCUMENT NUMBER: 134:86550
TITLE: Preparation of homogeneous polyoxime compounds by parallel assembly
INVENTOR(S): **Rose, Keith; Offord, Robin Ewart**
PATENT ASSIGNEE(S): Gryphon Sciences, USA
SOURCE: U.S., 36 pp., Cont.-in-part of U.S. Ser. No. 57,594, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6174530	B1	20010116	US 1993-114877	19930831
CA 2162157	AA	19941110	CA 1994-2162157	19940505
WO 9425071	A1	19941110	WO 1994-IB93	19940505
W: AT, AU, BR, CA, CH, CN, DE, DK, ES, FI, GB, HU, JP, LU, NL, NO, PL, RO, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
AU 9465438	A1	19941121	AU 1994-65438	19940505
AU 686153	B2	19980205		
EP 697891	A1	19960228	EP 1994-913192	19940505
EP 697891	B1	20000329		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08510210	T2	19961029	JP 1994-524080	19940505
JP 3734828	B2	20060111		
AT 191148	E	20000415	AT 1994-913192	19940505
ES 2146649	T3	20000816	ES 1994-913192	19940505
PT 697891	T	20000929	PT 1994-913192	19940505
GR 3033699	T3	20001031	GR 2000-401389	20000615
US 6663869	B1	20031216	US 2000-633269	20000804
PRIORITY APPLN. INFO.:			US 1993-57594	B2 19930505
			US 1993-105904	A 19930831
			US 1993-114877	A 19930831
			WO 1994-IB93	W 19940505
			US 1996-537928	A1 19960105

AB Homogeneous polyoximes of defined structure were prepared which comprise a baseplate structure having a plurality of oxime bonds, each of which links a specifically active mol. to the baseplate. Thus, parallel assembly of hexa-TCTP-polyoximes (TCTP = human translationally controlled tumor protein) by chemoselective ligation of a hexa-AOA-baseplate (AOA = aminooxyacetyl) and GXL-TCTP COSMs (GXL = glyoxylyl, COSMs = complementary orthogonal specifically active mol.) is described.

REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 6 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:572615 HCAPLUS

DOCUMENT NUMBER: 133:345631

TITLE: Positive and negative labeling of human proinsulin, insulin, and C-peptide with stable isotopes

AUTHOR(S): Stocklin, Reto; Arrighi, Jean-Francois; Hoang-Van, Khan; Vu, Lan; Cerini, Fabrice; Gilles, Nicolas; Genet, Roger; Markussen, Jan; **Offord, Robin E.** ; **Rose, Keith**

CORPORATE SOURCE: USA

SOURCE: Methods in Molecular Biology (Totowa, New Jersey) (2000), 146(Mass Spectrometry of Proteins and Peptides), 293-315
CODEN: MMBIED; ISSN: 1064-3745

PUBLISHER: Humana Press Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB This paper covers isotope dilution assay, stable isotope labeled analogs, neg. labeling, pharmacokinetic and metabolic studies, materials necessary, separation and extraction techniques, mass spectrometry, gene assembly, PCR, vectors, subcloning, plasmids, protein labeling procedures, protein modification, protein synthesis, anal. control, bioassay, peptide mapping, and high-resolution mass spectrometry.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 7 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:359045 HCAPLUS
DOCUMENT NUMBER: 133:134034
TITLE: Antibodies against thrombospondin-related anonymous protein do not inhibit Plasmodium sporozoite infectivity in vivo
AUTHOR(S): Gantt, Soren; Persson, Cathrine; **Rose, Keith**; Birkett, Ashley J.; Abagyan, Ruben; Nussenzweig, Victor
CORPORATE SOURCE: Department of Pathology, New York University School of Medicine, New York, NY, 10016, USA
SOURCE: Infection and Immunity (2000), 68(6), 3667-3673
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

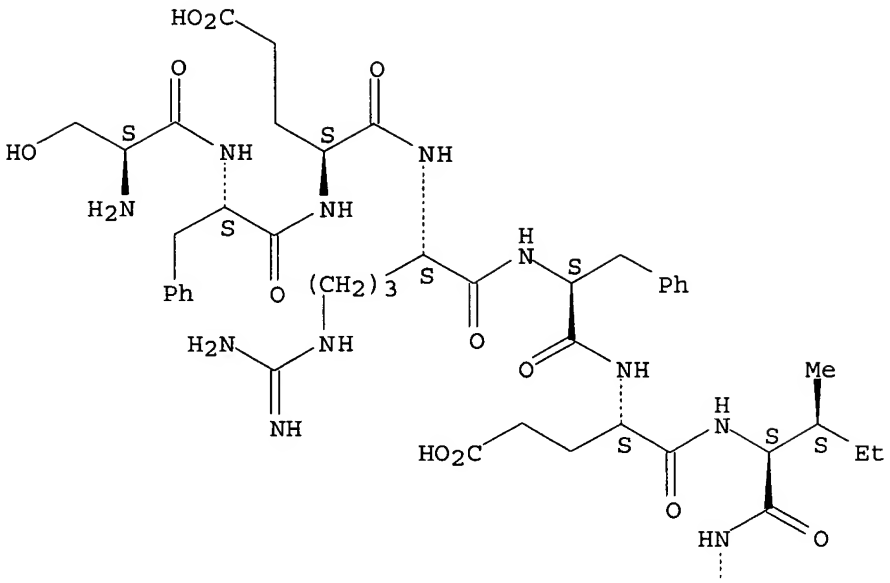
AB Thrombospondin-related anonymous protein (TRAP), a candidate malaria vaccine antigen, is required for Plasmodium sporozoite gliding motility and cell invasion. For the first time, the ability of antibodies against TRAP to inhibit sporozoite infectivity in vivo is evaluated in detail. TRAP contains an A-domain, a well-characterized adhesive motif found in integrins. We modeled here a three-dimensional structure of the TRAP A-domain of Plasmodium yoelii and located regions surrounding the MIDAS (metal ion-dependent adhesion site), the presumed business end of the domain. Mice were immunized with constructs containing these A-domain regions but were not protected from sporozoite challenge. Furthermore, monoclonal and rabbit polyclonal antibodies against the A-domain, the conserved N terminus, and the repeat region of TRAP had no effect on the gliding motility or sporozoite infectivity to mice. TRAP is located in micronemes, secretory organelles of apicomplexan parasites. Accordingly, the antibodies tested here stained cytoplasmic TRAP brightly by immunofluorescence. However, very little TRAP could be detected on the surface of sporozoites. In contrast, a dramatic relocalization of TRAP onto the parasite surface occurred when sporozoites were treated with calcium ionophore. This likely mimics the release of TRAP from micronemes when a sporozoite contacts its target cell in vivo. Contact with hepatoma cells in culture also appeared to induce the release of TRAP onto the surface of sporozoites. If large amts. of TRAP are released in close proximity to its cellular receptor(s), effective competitive inhibition by antibodies may be difficult to achieve.

IT **132031-49-3P**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(antibodies against thrombospondin-related anonymous protein in response to immunization with)

RN 132031-49-3 HCAPLUS
CN L-Glutamic acid, L-seryl-L-phenylalanyl-L-α-glutamyl-L-arginyl-L-phenylalanyl-L-α-glutamyl-L-isoleucyl-L-phenylalanyl-L-prolyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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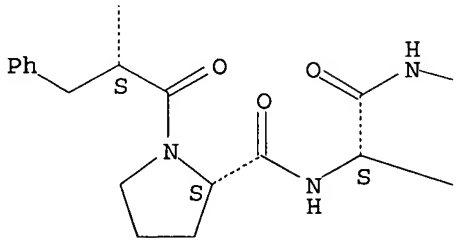
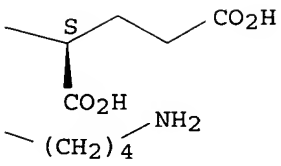


PAGE 2-B



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 8 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:794210 HCAPLUS

DOCUMENT NUMBER: 132:50249
TITLE: Preparation of hetero-polyoxime compounds by parallel assembly
INVENTOR(S): **Rose, Keith; Offord, Robin E.**
PATENT ASSIGNEE(S): Gryphon Sciences, USA
SOURCE: U.S., 43 pp., Cont.-in-part of U.S. Ser. No. 57,594, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6001364	A	19991214	US 1993-105904	19930831
CA 2162157	AA	19941110	CA 1994-2162157	19940505
WO 9425071	A1	19941110	WO 1994-IB93	19940505
W: AT, AU, BR, CA, CH, CN, DE, DK, ES, FI, GB, HU, JP, LU, NL, NO, PL, RO, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
AU 9465438	A1	19941121	AU 1994-65438	19940505
AU 686153	B2	19980205		
EP 697891	A1	19960228	EP 1994-913192	19940505
EP 697891	B1	20000329		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08510210	T2	19961029	JP 1994-524080	19940505
JP 3734828	B2	20060111		
AT 191148	E	20000415	AT 1994-913192	19940505
ES 2146649	T3	20000816	ES 1994-913192	19940505
PT 697891	T	20000929	PT 1994-913192	19940505
GR 3033699	T3	20001031	GR 2000-401389	20000615
US 6663869	B1	20031216	US 2000-633269	20000804

PRIORITY APPLN. INFO.:

US 1993-57594	B2	19930505
US 1993-105904	A	19930831
US 1993-114877	A	19930831
WO 1994-IB93	W	19940505
US 1996-537928	A1	19960105

AB Hetero-polyoximes of defined structure were prepared which comprise a baseplate structure having a plurality of oxime bonds, each of which links a specifically active mol. to the baseplate. Thus, parallel assembly of hexa-TCTP-polyoximes (TCTP = human translationally controlled tumor protein) by chemoselective ligation of a hexa-AOA-baseplate (AOA = aminooxyacetyl) and GXL-TCTP COSMs (GXL = glyoxylyl, COSMs = complementary orthogonal specifically active mol.) is described.
REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 9 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:618095 HCAPLUS
DOCUMENT NUMBER: 129:310982
TITLE: Short-term insulin-induced glycogen formation in primary hepatocytes as a screening bioassay for insulin action
AUTHOR(S): Vu, Lan; Pralong, William F.; Cerini, Fabrice; Gjinovci, Asllan; Stocklin, Reto; **Rose, Keith**; **Offord, Robin E.**; Kippen, Alistair D.
CORPORATE SOURCE: Department of Medical Biochemistry, University Medical Centre, Geneva, 1211/4, Switz.
SOURCE: Analytical Biochemistry (1998), 262(1), 17-22

CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors describe a novel bioassay to measure specific insulin-like activity in primary cultures of rat hepatocytes by determination of [3H]glycogen from D-[6-3H]glucose. The dose-response curve of insulin in this assay exhibited an EC50 of 0.42 (± 0.04) nM, which is comparable to the dissociation constant of insulin from its receptor in hepatocytes. The authors used this assay to examine possible residual insulin-like activity of the four major fragments formed upon insulin degradation by insulin protease. Fragments A1-13B1-19, A1-14B1-9, and A14-21B14-30 showed no measurable activity. Although prepns. of fragment A14-21B10-30 displayed dose-dependent agonist activity with an EC50 of 380 (± 40) nM, the authors conclude that this was due to an insulin-like impurity since the chemical synthesized fragment showed no such activity. In summary, this bioassay demonstrates the action of insulin on glycogen formation in hepatocytes and provides a rapid and sensitive measurement of insulin-like activity which could facilitate screening studies. (c) 1998 Academic Press.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 10 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:597589 HCAPLUS
DOCUMENT NUMBER: 129:290426
TITLE: Semisynthetic proteins with non-coded structural elements
AUTHOR(S): **Offord, R. E.**; Gaertner, H.; Proudfoot, A.; **Rose, K.**; Wells, T. N. C.; Werlen, R.
CORPORATE SOURCE: Departement de Biochimie Medicale, CMU, Geneva, 1211/4, Switz.
SOURCE: Peptides 1996, Proceedings of the European Peptide Symposium, 24th, Edinburgh, Sept. 8-13, 1996 (1998), Meeting Date 1996, 25-28. Editor(s): Ramage, Robert; Epton, Roger. Mayflower Scientific: Kingswinford, UK. CODEN: 66RCA5
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report. Amino-terminal and carboxy-terminal activation are discussed.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 11 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:351091 HCAPLUS
DOCUMENT NUMBER: 129:76142
TITLE: In vitro and in vivo comparison of a randomly coupled antibody fragment-enzyme conjugate with a site-specific conjugate
AUTHOR(S): Werlen, Raymond C.; **Offord, Robin E.**; Blakey, David C.; East, Simon J.; Melton, Roger G.; **Rose, Keith**
CORPORATE SOURCE: Departement de Biochimie Medicale, C.M.U., Geneva, CH 1211/4, Switz.
SOURCE: Biomedical Peptides, Proteins & Nucleic Acids (1995), 1(5), 251-254
CODEN: BPPAFS; ISSN: 1353-8616
PUBLISHER: Mayflower Worldwide

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two antibody fragment-enzyme conjugates, one obtained by random coupling of the two protein component, the other by site-specific ligation of the same component, were compared in vitro and in vivo for their usefulness in antibody directed enzyme prodrug therapy (ADEPT). The in vitro studies have shown that the site-specific conjugate has a higher antigen binding capacity, while both conjugates had similar specific enzymic activities. In vivo, the site-specific conjugate was cleared more rapidly. When correction was made for this faster clearance, both conjugates showed similar antitumor efficacy in a mouse xenograft system upon administration of a prodrug.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 12 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:249104 HCAPLUS
DOCUMENT NUMBER: 128:292242
TITLE: Elimination of free radionuclide by a chelating agent improves tumor-to-nontumor ratios following radioimmunotargeting with antibody labeled with 67Ga
AUTHOR(S): Ryser, J.-E.; **Rose, K.**; Jones, R.; Pelegrin, A.; Donath, A.; Egeli, R.; Smith, A.; **Offord, R. E.**
CORPORATE SOURCE: Div. Nuclear Med., Univ. Med. Cent., Geneva, Switz.
SOURCE: Nuclear Medicine and Biology (1998), 25(3), 261-265
CODEN: NMBIEO; ISSN: 0969-8051
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To circumvent radionuclide accumulation in nontarget tissues when employing metallic radionuclides for radioimmunoscintigraphy or radioimmunotherapy, we have investigated the effect of the chelating agent deferroxamine (DFO) on the biodistribution of 67Ga following its administration attached to intact monoclonal antibody MAb35 and its F(ab'')2 fragment. Following administration of 67Ga-labeled MAb35, DFO accelerated whole-body elimination of 67Ga and reduced its accumulation in several normal tissues, including liver, spleen and kidney. No reduction in tumor accumulation of 67Ga was observed Following administration of 67Ga-labeled F(ab')2 fragment, kidney accumulation was higher than with the intact antibody (29% and 4% ID/g, resp.) and blood levels lower (0.69% and 5% ID/g, resp.). Again, no alteration in tumor accumulation of 67Ga was seen following DFO, although liver, kidney and blood levels were reduced and whole-body elimination accelerated.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 13 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:318723 HCAPLUS
DOCUMENT NUMBER: 127:29195
TITLE: Development of an isotope dilution assay for precise determination of insulin, C-peptide, and proinsulin levels in non-diabetic and type II diabetic individuals with comparison to immunoassay
AUTHOR(S): Kippen, Alistair D.; Cerini, Fabrice; Vadas, Laszlo; Stocklin, Reto; Vu, Lan; **Offord, Robin E.**; **Rose, Keith**
CORPORATE SOURCE: Department Medical Biochemistry, University Medical Centre and Central Laboratory Clinical Chemistry, University Hospital, Geneva, 1211, Switz.

SOURCE: Journal of Biological Chemistry (1997), 272(19), 12513-12522
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We describe the application of a stable isotope dilution assay (IDA) to determine precise insulin, C-peptide, and proinsulin levels in blood by extraction from serum and quantitation by mass spectrometry using analogs of each target protein labeled with stable isotopes. Insulin and C-peptide levels were also determined by immunoassay, which gave consistently higher results than by IDA, the relative difference being larger at low concns. Insulin, C-peptide, and proinsulin levels were all shown by IDA to be higher in type II diabetics than in non-diabetics, with mean values rising from 22 (±2) to 92 (±8), 335 (±11) to 821 (±24), and 6 (±1) to 37 (±3) pM, resp. Interestingly, the ratio between IDA and immunoassay values for insulin levels increased from 1.3 in non-diabetics to 1.7 in type II diabetics. The ratio between proinsulin and insulin levels by IDA increased from 0.24 in non-diabetics to 0.36 in type II diabetics, whereas the ratio between C-peptide and insulin levels by IDA decreased from 17.6 to 10.7. This disproportionate change in protein levels between different types of individuals has implications for the metabolism of insulin in the diabetics studied (type II) and suggests that C-peptide levels are not always a reliable guide as to pancreatic insulin secretion. In addition, levels of the 33-residue C-peptide (partially trimmed form) were shown to be less than 10% that of the fully trimmed 31-residue C-peptide levels, and we tested IDA in a clin. context by two post-pancreatic graft studies. IDA was shown to give direct, pos. identification of the target protein with unrivaled accuracy, avoiding many of the problems associated with present methodol. for protein determination
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 14 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:4643 HCAPLUS
DOCUMENT NUMBER: 126:84752
TITLE: A stable isotope dilution assay for the in vivo determination of insulin levels in humans by mass spectrometry
AUTHOR(S): Stocklin, Reto; Vu, Lan; Vadas, Laszlo; Cerini, Fabrice; Kippen, Alistair D.; **Offord, Robin E.** ; **Rose, Keith**
CORPORATE SOURCE: Dept. of Medical Biochemistry, Univ. of Geneva Medical Center, Geneva, Switz.
SOURCE: Diabetes (1997), 46(1), 44-50
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Insulin levels in humans were measured by a new assay, the isotope dilution assay (IDA), based on stable isotope dilution mass spectrometry. A known amount of a deuterated analog of insulin was used as an internal standard and added to the serum samples before sample processing. After isolation by immunoaffinity chromatog. and solid phase extraction, followed by a purification step on reversed-phase microbore high-performance liquid chromatog. (HPLC), the insulin-containing fraction was analyzed by mass spectrometry. The relative intensity of the signals due to insulin and its deuterated analog

in the mass spectrum was used to determine the concentration of insulin in the sample.
Using serum samples of 0.5-2.0 mL, we were able to measure insulin levels in the range of 3-1700 pmol/l in several clin. samples from type II diabetic patients. The basal level of endogenous insulin was also determined in two normal subjects and found to be .apprx.20pmol/l. Insulin secretion was followed after the ingestion of 75 g glucose in one healthy volunteer. Finally, the determination of the insulin level of one hemolyzed post-mortem blood
sample, for which immunoassays gave inconsistent results, was performed to help forensic investigations. Our results showed a good correlation with standard immunoassay data, except in six samples where much lower values were obtained by our stable isotope dilution assay, suggesting an overestimation of insulin levels by immunoassay in some cases. As it is not subject to immunol. interferences by insulin-related compds., this new assay has a major clin. advantage in that it avoids confusions related to hyperinsulinemia.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 15 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:695771 HCAPLUS
DOCUMENT NUMBER: 126:4152
TITLE: Chemical ligation of proteins and other macromolecules
AUTHOR(S): Gaertner, H. F. G.; Werlen, R. C.; **Offord, R. E.; Rose, K.**
CORPORATE SOURCE: Gryphon Sciences, San Francisco, CA, 94080, USA
SOURCE: Peptides: Chemistry, Structure and Biology, Proceedings of the American Peptide Symposium, 14th, Columbus, Ohio, June 18-23, 1995 (1996), Meeting Date 1995, 18-20. Editor(s): Kaumaya, Pravin T. P.; Hodges, Robert S. Mayflower Scientific: Kingswinford, UK.
CODEN: 63NTAF
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A method for the controlled joining of unprotected proteins or protein fragments to give defined structures with a contiguous main chain or, alternatively, a means of protein labeling in which one substitution only per mol. will take place and at a determined site is described.

L23 ANSWER 16 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:104633 HCAPLUS
DOCUMENT NUMBER: 124:225169
TITLE: Preparation of a trivalent antigen-binding construct using polyoxime chemistry: improved biodistribution and potential for therapeutic application
AUTHOR(S): Werlen, Raymond C.; Lankinen, Mervi; **Offord, Robin E.**; Schubiger, P. August; SMith, Alan; **Rose, Keith**
CORPORATE SOURCE: Dep. Medical Biochem., Centre Medical Universitaire, Geneva, CH-1211, Switz.
SOURCE: Cancer Research (1996), 56(4), 809-15
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To improve the pharmacokinetic behavior of an antitumor radioimmunoconjugate, we have prepared a trivalent antigen-binding construct formed from three Fab' fragments derived from the parent murine monoclonal

antibody (MAb) 35 directed against the carcinoembryonic antigen. The construct was generated by a novel approach using polyoxime chemical This approach leads to a homogeneous construct, as judged by SDS-PAGE and by mass spectrometry, which was found to retain full immunoreactivity. A comparison of the monovalent, divalent, and trivalent F(ab')n materials in vitro revealed the expected trend of increasing association constant with increasing valency. The in vivo biodistribution of the 125I-labeled trivalent construct was studied in xenograft-bearing nude mice. Absolute tumor accumulation seen with the trivalent construct (10.8% injected dose/g) was lower than that seen with the intact MAb35 (15.2% injected dose/g). This finding and the more rapid loss of activity from tumor are presumably the consequence of the quicker blood clearance of the trivalent material. However, the construct showed tumor:blood ratios up to 10-fold higher than those seen for the parent antibody, and ratios of tumor:normal tissue accumulation were generally greatly improved. These improvements were achieved despite only modest reduction in maximum tumor accumulation when compared to the parent MAb35, and this argues well for an improved potential for this novel construct as an agent for radioimmunotherapy and radioimmunoscintigraphy.

L23 ANSWER 17 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:83878 HCAPLUS
DOCUMENT NUMBER: 124:172723
TITLE: Site-specific immunoconjugates
AUTHOR(S): Werlen, R. C.; Lankinen, M.; Smith, A.; Chernushevich, I.; Standing, K. G.; Blakey, D. C.; Shuttleworth, H.; Melton, R. G.; **Offord, R. E.**; **Rose, K.**
CORPORATE SOURCE: Dep. Biochim. Med., Centre Med. Univ., Geneca, CH-1211, Switz.
SOURCE: Tumor Targeting (1995), 1(5), 251-8
CODEN: TUTAF9; ISSN: 1351-8488
PUBLISHER: Chapman & Hall
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with 19 refs. The conjugation of two proteins with different activities in order to get a conjugate with a new hybrid activity is a field of intense investigation. The standard way of preparing such conjugates uses random acylation of lysine side-chains with heterobifunctional reagents, leading to a mixture of conjugates where both protein partners are linked to one another in different orientations. To circumvent this difficulty, we are developing precise conjugation techniques for the preparation of site-specific protein conjugates. Here we review the preparation, characterization and the use of three such site-specific immunoconjugates: an antibody fragment-enzyme conjugate designed for ADEPT (antibody-directed enzyme prodrug therapy) and two F(ab')3 constructions prepared with different linkers. The ADEPT conjugate is a head-to-tail conjugate between an F(ab')3 antibody fragment and the enzyme carboxypeptidase G2 (CPG2). The components are linked through the formation of a hydrazone bond between a carbohydrazide, introduced at the C-terminus of the truncated heavy chain of the antibody fragment by reverse proteolysis, and an aldehyde, obtained by mild periodate oxidation of a threonine introduced at the N-terminus of the CPG2 by genetic engineering. This conjugate has been characterized by ESI-TOF (electrospray ionization time of flight) mass spectrometry and its in vitro and in vivo behavior was compared with that of a corresponding random conjugate. For the preparation of both F(ab')3 constructions, an Fab with a single thiol group was first prepared by digestion with appropriate proteases. In the first case, the thiol was then converted to an aminooxy

group. A trivalent construct was then obtained by polyoxime formation with a trialdehyde template. This F(ab')3 has been characterized by ESI-TOF mass spectrometry and its biodistribution in tumor-bearing mice has been investigated. The second F(ab')3 was obtained starting with the same Fab, but the trivalent construct was prepared on a template containing two aldehydes and a maleimide group, allowing the introduction of three Fab in three different steps.

L23 ANSWER 18 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:340859 HCAPLUS
DOCUMENT NUMBER: 122:133873
TITLE: Polyoxime compounds, their preparation, and their use for cell imaging and in vaccines
INVENTOR(S): **Rose, Keith; Offord, Robin E.**
PATENT ASSIGNEE(S): Switz.
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9425071	A1	19941110	WO 1994-IB93	19940505
W: AT, AU, BR, CA, CH, CN, DE, DK, ES, FI, GB, HU, JP, LU, NL, NO, PL, RO, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
US 6001364	A	19991214	US 1993-105904	19930831
US 6174530	B1	20010116	US 1993-114877	19930831
AU 9465438	A1	19941121	AU 1994-65438	19940505
AU 686153	B2	19980205		
EP 697891	A1	19960228	EP 1994-913192	19940505
EP 697891	B1	20000329		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08510210	T2	19961029	JP 1994-524080	19940505
JP 3734828	B2	20060111		
AT 191148	E	20000415	AT 1994-913192	19940505
US 6217873	B1	20010417	US 1996-537928	19960105
GR 3033699	T3	20001031	GR 2000-401389	20000615
US 6663869	B1	20031216	US 2000-633269	20000804
US 2005025740	A1	20050203	US 2003-687711	20031020

PRIORITY APPLN. INFO.:		
US 1993-57594	A	19930505
US 1993-105904	A	19930831
US 1993-114877	A	19930831
WO 1994-IB93	W	19940505
US 1996-537928	A1	19960105
US 2000-633269	A1	20000804

AB Provided by this invention are essentially homogeneous, defined compns. of matter and hetero-polyoximes of defined structure comprising a baseplate structure having a plurality of oxime bonds, wherein each oxime bond links a specifically active mol. (e.g., a bioactive peptide)to the baseplate. Also provided are novel baseplates having a plurality of oxime-forming complementary reactive groups and novel specifically reactive mols. having a oxime-forming complementary reactive group. Addnl., methods are described for preparing these novel compns. by chemoselectively ligating via oxime bond formation a complementary orthogonal reactive group on the baseplate to a complementary reactive orthogonal group on a specifically active mol. Pharmaceutical compns. containing these polyoximes and methods of inducing an immune response or of imaging cells with the polyoximes are

claimed. Baseplate structures containing aminooxyacetyl (AOA) or glyoxylyl (GLX) reactive groups and peptides with complementary reactivity, i.e., peptides containing GLX or AOA termini, were prepared The polyoximes were formed by reaction of the baseplates and peptide derivs.

L23 ANSWER 19 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:131398 HCAPLUS
DOCUMENT NUMBER: 122:75865
TITLE: High Yield, Site-Specific Coupling of N-Terminally Modified β-Lactamase to a Proteolytically Derived Single-Sulfhydryl Murine Fab'
AUTHOR(S): Mikolajczyk, Stephen D.; Meyer, Damon L.; Starling, James J.; Law, Kevin L.; **Rose, Keith**; Dufour, Brigitte; **Offord, Robin E.**
CORPORATE SOURCE: Hybritech Incorporated, San Diego, CA, 92196-9006, USA
SOURCE: Bioconjugate Chemistry (1994), 5(6), 636-46
CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The preparation of bispecific protein conjugates capable of performing diverse biol. functions is an area of active investigation. Such conjugates are routinely prepared using techniques which employ random derivatization of lysine residues, but the overall utility of these methods is limited due to poor yields and heterogeneous conjugates. In this report the authors describe the development of site-specific linkage methodol. for the chemical synthesis of a homogeneous enzyme-antibody Fab' conjugate with coupling efficiencies of at least 72%. The N-terminal threonine residue of β-lactamase from the P99 strain of Enterobacter cloacae was oxidized to an aldehyde functional group under mild conditions with a 5-fold molar excess of sodium periodate. The murine Fab' with a single sulfhydryl at the hinge region was generated by further digestion of the peptic Fab' fragment with lysyl endopeptidase to remove a decapeptide containing two of the three cysteine residues. Coupling of the two modified proteins was accomplished through a bifunctional coupling reagent containing maleimide and aminooxy functional groups. Synthesis of the linker is described. Yields of 1:1 enzyme-Fab' were at least three times higher than for comparable random derivatization methods. Immunoreactivity and enzymic activity were unaffected. Biodistribution studies showed a more favorable tumor to blood ratio with the site-specifically linked conjugate.

L23 ANSWER 20 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:66885 HCAPLUS
DOCUMENT NUMBER: 122:10667
TITLE: Reverse proteolysis as a means of introducing non-coded changes into proteins
AUTHOR(S): **Offord, R. E.**; Fisch, I.; Gaertner, H. F.; **Rose, K.**
CORPORATE SOURCE: Departement de Biochimie Medicale, Centre Medical Universitaire, Geneva, CH-1211, Switz.
SOURCE: Pept. 1992, Proc. Eur. Pept. Symp., 22nd (1993), Meeting Date 1992, 38-40. Editor(s): Schneider, Conrad H.; Eberle, Alex N. ESCOM: Leiden, Neth.
CODEN: 60LUAN
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A report from a symposium.

L23 ANSWER 21 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:13705 HCAPLUS
DOCUMENT NUMBER: 122:10665

TITLE: Site-Specific Religation of G-CSF Fragments through a Thioether Bond
AUTHOR(S): Gaertner, Hubert F.; **Offord, Robin E.**; Cotton, Ron; Timms, David; Camble, Roger; **Rose, Keith**
CORPORATE SOURCE: Departement de Biochimie Medicale, Centre Medical Universitaire, Geneva, 1211, Switz.
SOURCE: Bioconjugate Chemistry (1994), 5(4), 333-8
CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new approach is described for linking, through a thioether bond,the C-terminus of one unprotected peptide with the N-terminus of a another. Homocysteine thiolactone is attached to the C-terminus of one peptide by reverse proteolysis and provides through hydroxylamine treatment a free sulfhydryl group. The α-amino group of a second peptide is selectively iodoacetylated by reaction with iodoacetic anhydride at pH 6.0 or the N-hydroxysuccinimide ester derivative at pH 7.0. Coupling of the two modified fragments occurs in a spontaneous alkylation reaction under mild conditions. After preliminary expts. with small peptides, this approach was extended to large protein fragments derived from recombinant analogs of G-CSF by enzymic digestion. This approach provides a means of making head-to-tail protein chimeras or introducing noncoded structural elements into a protein.

L23 ANSWER 22 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:681214 HCAPLUS
DOCUMENT NUMBER: 121:281214
TITLE: Construction of protein analogs by site-specific condensation of unprotected fragments
AUTHOR(S): Gaertner, H. F.; **Rose, K.**; Cotton, R.; Timms, D.; Camble, R.; **Offord, R. E.**
CORPORATE SOURCE: C.M.U., Geneva, CH-1211, Switz.
SOURCE: Pept. 1992, Proc. Eur. Pept. Symp., 22nd (1993), Meeting Date 1992, 239-40. Editor(s): Schneider, Conrad H.; Eberle, Alex N. ESCOM: Leiden, Neth.
CODEN: 60LUAN
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A report from a symposium on the semisynthesis of protein analogs via hydrazone formation between a peptide C-terminal hydrazide and an aldehyde formed selectively from periodate oxidation of an N-terminal serine peptide. The oxidation step was optimized to preclude any modification of methionine residues.

L23 ANSWER 23 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:631351 HCAPLUS
DOCUMENT NUMBER: 121:231351
TITLE: Synthesis and use of a defined oligomer for targeted drug therapy
AUTHOR(S): Vilaseca, L. A.; **Rose, K.**; Werlen, R.; Meunier, A.; **Offord, R. E.**; Nichols, C. L.; Scott, W. L.
CORPORATE SOURCE: CMU, Geneva, CH-1211, Switz.
SOURCE: Pept. 1992, Proc. Eur. Pept. Symp., 22nd (1993), Meeting Date 1992, 819-20. Editor(s): Schneider, Conrad H.; Eberle, Alex N. ESCOM: Leiden, Neth.
CODEN: 60LUAN
DOCUMENT TYPE: Conference
LANGUAGE: English

AB New synthetic oligomers are prepared which permit the attachment, to a single site, of a cluster of drug mols. to antibodies or their fragments for use in targeted drug therapy.

L23 ANSWER 24 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:599269 HCAPLUS
DOCUMENT NUMBER: 121:199269
TITLE: Preparation and characterization of novel substrates of insulin proteinase (EC 3.4.99.45)
AUTHOR(S): Werlen, Raymond Charles; **Offord, Robin Ewart**; **Rose, Keith**
CORPORATE SOURCE: Department Biochimie Medicale, C.M.U., Geneva, CH 1211, Switz.
SOURCE: Biochemical Journal (1994), 302(3), 907-11
CODEN: BIJOAK; ISSN: 0264-6021
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The specificity of insulin proteinase (EC 3.4.99.45) has been difficult to categorize using only it natural substrates. By exploiting the fact that two substrates competing for the same enzyme inhibit one another, the authors have found some new substrates of the insulin proteinase from porcine muscle. Two of these substrates, a tryptic fragment of BSA and a fragment of cytochrome c, have been shown to be cleaved at a single site. The albumin fragment, as well as another fragment of cytochrome c, have susceptibilities (Vmax/Km) comparable with that of insulin. In a second aspect of the study, the porcine-muscle enzyme was shown to be related to other members of its superfamily in that it was immunopptd. by a monoclonal antibody raised against the insulin-degrading enzyme from human red blood cells and has the same cleavage sites on insulin as has the rat skeletal-muscle insulin proteinase. The authors note, however, a possible discrepancy between the results and those of another group regarding the subunit size (110 kDa) of the immunopptd. material.

L23 ANSWER 25 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:563795 HCAPLUS
DOCUMENT NUMBER: 121:163795
TITLE: Site-Specific Conjugation of an Enzyme and an Antibody Fragment
AUTHOR(S): Werlen, Raymond C.; Lankinen, Mervi; **Rose, Keith**; Blakey, David; Shuttleworth, Helen; Melton, Roger; **Offord, Robin E.**
CORPORATE SOURCE: Departement de Biochimie Medicale, Centre Medical Universitaire, Geneva, CH 1211, Switz.
SOURCE: Bioconjugate Chemistry (1994), 5(5), 411-17
CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A site-specific immunoconjugate was prepared between a F(ab')2-like fragment of the monoclonal anti-CEA murine IgG1 A5B7 and a mutant of the dimeric enzyme carboxypeptidase G2 possessing an N-terminal Thr in place of Ala. First an aldehyde was introduced at the N-terminus of the enzyme by mild periodate oxidation and a residue of carbohydrazide was specifically introduced at the C-terminus of the truncated heavy chain of the F(ab')2-like fragment by reverse proteolysis. Then the two modified proteins were conjugated by the formation of a hydrazone bond between the hydrazide and the aldehyde groups. The conjugate obtained retained both enzymic activity and antigen-binding capacity. The antigen-binding capacity was better than that of a similar conjugate made conventionally by random reaction with side chains.

L23 ANSWER 26 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:430352 HCAPLUS
DOCUMENT NUMBER: 121:30352
TITLE: Chemo-enzymic backbone engineering of proteins. Site-specific incorporation of synthetic peptides that mimic the 64-74 disulfide loop of granulocyte colony-stimulating factor
AUTHOR(S): Gaertner, Hubert F.; **Offord, Robin E.**; Cotton, Ron; Timms, David; Camble, Roger; **Rose, Keith**
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, 1211, Switz.
SOURCE: Journal of Biological Chemistry (1994), 269(10), 7224-30
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors present the concept of chemo-enzymic backbone engineering of proteins. Recombinant DNA techniques are used to produce appropriate proteins that are enzymically fragmented to give the starting materials. These fragments are modified specifically at their chain termini either enzymically (coupling of a hydrazide to the C terminus) or chemical (periodate oxidation of N-terminal serine to a glyoxylyl function). The modified fragments, which need no side protection whatever, are mixed together and religate themselves spontaneously under mild conditions. The hydrazone bond thus formed can be reduced if desired, which stabilizes the linkage and enhances the flexibility of the local conformation. In this way biol. or chemical derived structures can be incorporated into the protein, and the choice of the chemical ones is free of all of the constraints of the genetic code. The authors believe that this combined approach gives access to constructions that could not be derived by either recombinant or chemical methods alone. The authors illustrate the particularity of this concept by the engineered modifications of the 64-74 disulfide loop region of human granulocyte colony-stimulating factor. Analogs constructed include one which, in spite of having a nonpeptide link in its backbone, has full biol. activity.

L23 ANSWER 27 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:183131 HCAPLUS
DOCUMENT NUMBER: 120:183131
TITLE: This semisynthesis of [octadeutero-PheB1-octadeutero-ValB2]-porcine insulin and its characterization by mass spectrometry
AUTHOR(S): Stoecklin, Reto; **Rose, Keith**; Green, Brian N.; **Offord, Robin E.**
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, 1211, Switz.
SOURCE: Protein Engineering (1994), 7(2), 285-9
CODEN: PRENE9; ISSN: 0269-2139
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Insulin analogs labeled with stable isotopes (e.g. deuterium, 18O, 15N, etc.) are authentic (the native structure is rigorously maintained), non-radioactive (preferred for injection into man) and can easily be distinguished from endogenous insulin by mass spectrometry by virtue of their mol. masses. Appropriate combinations of amino-protecting groups (methylsulfonylethyloxycarbonyl and t-butoxycarbonyl), Edman degradation and chemical coupling were used to produce [octadeutero-PheB1]-porcine insulin and [octadeutero-PheB1-octadeutero-ValB2]-porcine insulin. The analogs were characterized by electrospray ionization mass spectrometry. Standard

mixts. of labeled and unlabeled insulins were successfully studied by mass spectrometry. Isotope dilution mass spectrometry could therefore provide a useful direct measure of insulin under true physiol. conditions, without many of the drawbacks of existing methods. In this regard, the analog with 16 deuteriums was more suitable than the octadeuterated analog, since the greater mass difference between the labeled and unlabeled forms enabled a lower mass spectrometric resolution to be used, resulting in higher sensitivity.

L23 ANSWER 28 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:46328 HCAPLUS
DOCUMENT NUMBER: 120:46328
TITLE: Facile identification by electrospray mass spectrometry of the insulin fragment A14-21-B17-30 produced by insulin proteinase
AUTHOR(S): Vu, Lan; Stoecklin, Reto; **Rose, Keith**; **Offord, Robin E.**
CORPORATE SOURCE: Dep. de Biochim. Med., Cent. Med. Univ., Geneva, 1211, Switz.
SOURCE: Rapid Communications in Mass Spectrometry (1993), 7(11), 1048-50
CODEN: RCMSEF; ISSN: 0951-4198
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors confirm the cleavage at position B16-17 of porcine insulin which occurs during in vitro digestion by insulin proteinase. The fragment A14-21-B17-30 was purified by reversed-phase high performance liquid chromatog. and characterized by electrospray ionization mass spectrometry. Fast-atom bombardment mass spectrometry, failed to detect the presence of this fragment.

L23 ANSWER 29 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:38047 HCAPLUS
DOCUMENT NUMBER: 120:38047
TITLE: Protein conjugates of defined structure: Synthesis and use of a new carrier molecule
AUTHOR(S): Vilaseca, L. Antonio; **Rose, Keith**; Werlen, Raymond; Meunier, Anne; **Offord, Robin E.**; Nichols, Cynthia L.; Scott, William L.
CORPORATE SOURCE: Cent. Med. Univ., Geneva, CH 1211, Switz.
SOURCE: Bioconjugate Chemistry (1993), 4(6), 515-20
CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new carrier mol., NH2OCH2CO-(Gly)3-[Lys(H-Ser-)]5-Gly-OH, was synthesized to facilitate the preparation of protein conjugates of defined structure. Special features are as follows: (i) (aminooxy)acetyl as a terminal group, which reacts specifically to form an oxime bond under very mild conditions with an aldehyde group placed on a protein in a prior step; (ii) a spacer group of three Gly residues; and (iii) a set of 5 Lys residues, each of which is acylated with a Ser residue. A second form of the carrier mol., HCO-m-C6H4CH:NOCH2CO-(Gly)3-[Lys(H-Ser)]5-Gly-OH, was also prepared This form has a terminal aldehyde group which permits site-specific attachment by formation of a hydrazone bond to the carboxyl termini of polypeptide chains which have been modified enzymically with carbohydrazide in a prior step. Once the carrier is linked to protein in one of the above ways, i.e. through formation of either an oxime or hydrazone bond, the Ser residues of the carrier (but not the protein) may be oxidized by very mild periodate treatment to generate aldehyde groups. Drugs possessing a hydrazide group (e.g. methotrexate γ-hydrazide or

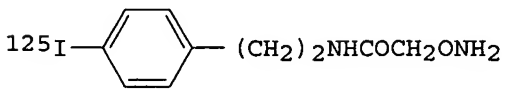
desacetylvincaleukoblastine hydrazide) may then be conjugated via hydrazone formation to the aldehyde groups of the carrier. A cluster of 5-drug mols. may thus be attached to a single site on a protein, giving a relatively homogeneous product in spite of the high drug conjugation ratio. Synthesis of the carrier, formation of a pentadrug-protein conjugate, and wider implications of the chemical are presented.

L23 ANSWER 30 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:415327 HCAPLUS
DOCUMENT NUMBER: 119:15327
TITLE: Cluster conjugates of drugs with antibodies
INVENTOR(S): Koppel, Gary Allen; **Offord, Robin E.**; **Rose, Keith**; Scott, William Leonard
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 33 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 525992	A2	19930203	EP 1992-306052	19920630
EP 525992	A3	19940316		
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL, PT, SE				
US 5272253	A	19931221	US 1991-724030	19910701
CA 2072824	AA	19930102	CA 1992-2072824	19920630
JP 05238952	A2	19930917	JP 1992-172624	19920630

PRIORITY APPLN. INFO.: US 1991-724030 A 19910701
OTHER SOURCE(S): MARPAT 119:15327
AB Cytotoxic drugs are conjugated with antibodies through a linker to target the cancer cells. Antibody 007B F(ab')2 fragments were prepared, reacted with carbohydrazide and peptide crosslinker, and conjugated with 4-desacetyl-23-desmethoxyvinblastine-23-hydrazide.

L23 ANSWER 31 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:229328 HCAPLUS
DOCUMENT NUMBER: 118:229328
TITLE: Site-specific conjugation of a radioiodinated phenethylamine derivative to a monoclonal antibody results in increased radioactivity localization in tumor
AUTHOR(S): Kurth, Mark; Pelegrin, Andre; **Rose, Keith**; **Offord, Robin E.**; Pochon, Sibylle; Mach, Jean Pierre; Buchegger, Franz
CORPORATE SOURCE: Dep. Chem., Univ. California, Davis, CA, 95616, USA
SOURCE: Journal of Medicinal Chemistry (1993), 36(9), 1255-61
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The preparation of a novel radioiodination reagent, the (aminooxy)acetyl derivative (I) of (p-[125I]iodophenyl)ethylamine, is described. Conventional radioiodination of proteins involves the formation of iodotyrosine residues, but for in vivo applications such as thyroid or stomach immunoscintigraphy, the susceptibility of these residues to tissue dehalogenases constitutes a serious disadvantage. Using this new compound, which has a particularly nonreactive aromatic ring, studies were confirmed indicating the much greater in vivo stability of iodophenyl compds. compared to the more conventional iodophenolic ones. In addition, the aminooxy group of I gives a stable and specific linkage to aldehyde groups formed by periodate oxidation on the sugar moiety of antibody mols. In vitro, favorable binding activity and high stability was obtained with a I-labeled monoclonal antibody directed against carcinoembryonic antigen. In vivo, using paired labeling expts. in nude mice bearing colon carcinoma xenografts, the ({[125I]iodoaryl}amino)oxy-MAb (MAb = monoclonal antibody) was compared with the same MAb 131I-labeled by the conventional chloramine-T method. Tumor 125I concentration of (arylamino)oxy MAb (measured as percent injected dose per g) was higher as compared to values obtained with a conventionally labeled 131I antibody. Addnl., thyroid uptake, an indicator of iodine release from the antibody, was up to 25-fold lower after injection of 125I-MAb obtained by the new method as compared to the conventionally iodinated 131I-MAb.

L23 ANSWER 32 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1992:251555 HCAPLUS
DOCUMENT NUMBER:	116:251555
TITLE:	Construction of protein analogs by site-specific condensation of unprotected fragments
AUTHOR(S):	Gaertner, Hubert F.; **Rose, Keith**; Cotton, Ron; Timms, David; Camble, Roger; **Offord, Robin E.**
CORPORATE SOURCE:	Dep. Biochim. Med., Cent. Med. Univ., Geneva, 1211, Switz.
SOURCE:	Bioconjugate Chemistry (1992), 3(3), 262-8 CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The extreme sensitivity to periodate of 1-amino, 2-hydroxy compds. permits the selective conversion of N-terminal serine and threonine to an aldehydic group. The authors have used this reaction to construct analogs of human granulocyte colony stimulating factor (G-CSF) by allowing such oxidized peptides to react with others that have had a hydrazide derivative attached to the C-terminus by reversed proteolysis. Two recombinant analogs of G-CSF were used as starting materials. Both had only a single lysine residue (at position 62 and 75, resp.) followed immediately by a serine. Digestion of each analog by the lysine-specific protease from Achromobacter lyticus gave two fragments, one of which could be N-terminally oxidized and the other converted to the C-terminal hydrazide derivative by reversed proteolysis using the same enzyme. After preliminary studies with model peptides, they first reacted the corresponding peptide pairs together and then, in order to eliminate the 64-74 disulfide loop, fragment 1-62 from the first analog with fragment 76-174 from the second. Reactions are efficient (up to 80% product based on the oxidized fragment) and take place under very mild conditions. The hydrazone bond can easily be stabilized by reduction with NaBH3CN. This method represents a new, reasonably general route for the construction of large protein chimeras of precisely controlled structure.

L23 ANSWER 33 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:152401 HCAPLUS
DOCUMENT NUMBER: 116:152401
TITLE: Preparation of functionalized polyaminocarboxylic acid derivatives and their conjugates with biomolecules
INVENTOR(S): **Offord, Robin Ewart; Rose, Keith**
PATENT ASSIGNEE(S): Switz.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9113097	A1	19910905	WO 1991-GB316	19910228
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				

PRIORITY APPLN. INFO.: GB 1990-4538 A 19900228
AB RXnNHCOR1 [R = N-linked polyaminocarboxylic acid residue; X = spacer group; n = 0, 1; R1 = reactive functional group (e.g., CHO) capable of selective reaction with thiol, amino, carboxyl, hydroxyl, aldehyde, or (hetero)aromatic groups], and their conjugates with proteins, peptides, or carbohydrates, were prepared Thus, polyglutamic acid was coupled to BOC-NHOCH2CO-ONSu (BOC = Me3CO2C, Su = succinimidyl) using 1-hydroxybenzotriazole in Me2SO/N-ethylmorpholine. The product was activated with 1,1-carbonyldiimidazole and condensed with ferrioxamine to give BOC-NHOCH2CO-PG(ferrioxamine), (PG = polyglutamyl) where .apprx.77% of the PG carboxyls were substituted. The latter was deprotected and coupled with an aldehydic monoclonal antibody.

L23 ANSWER 34 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:147017 HCAPLUS
DOCUMENT NUMBER: 116:147017
TITLE: Site-specific modification of a fragment of a chimeric monoclonal antibody using reverse proteolysis
AUTHOR(S): Fisch, Igor; Kunzi, Gabriel; **Rose, Keith**; **Offord, Robin E.**
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, 1211, Switz.
SOURCE: Bioconjugate Chemistry (1992), 3(2), 147-53
CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel method is proposed for the site-specific labeling of antibodies under mild conditions and, as an example, the modification is given of an F(ab')2-like fragment of the chimeric monoclonal antibody B72.3. The F(ab')2-like fragment was produced by the action of the protease lysyl endopeptidase. Reverse proteolysis, catalyzed by the same enzyme, was then used to attach carbohydrazide specifically to the carboxyl termini of the heavy chains of the fragment. Finally, a radiolabeled chelator possessing an aldehyde group was conjugated to the modified fragment through a hydrazone linkage. The resulting site-specifically labeled F(ab')2-like fragment was characterized by gel electrophoresis and by enzymic digestion. It had immunoreactivity equivalent to that of the unmodified F(ab')2-like fragment as determined by immunofluorescence and ELISA techniques. The advantages and disadvantages of this labeling method, which appear to be of quite general applicability, are discussed.

L23 ANSWER 35 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:2891 HCAPLUS
DOCUMENT NUMBER: 116:2891
TITLE: Site-specific modification of antibodies by enzyme-assisted reverse proteolysis
AUTHOR(S): Fisch, I.; Pochon, S.; Werlen, R.; Jones, R. M. L.; **Rose, K.; Offord, R. E.**
CORPORATE SOURCE: CMU, Geneva, CH-1211, Switz.
SOURCE: Pept. 1990, Proc. Eur. Pept. Symp., 21st (1991), Meeting Date 1990, 819-21. Editor(s): Giralt, Ernest; Andreu, David. ESCOM Sci. Publ.: Leiden, Neth. CODEN: 57HNAI
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Protein modification by enzyme-assisted reverse proteolysis has been extended to large fragments of antibodies. The approach permits the site-specific attachment of a labeled chelator to the F(ab)'2-like fragment derived from the chimeric antibody B72.3 by treatment with lysyl endopeptidase. Reverse proteolysis has been successfully applied to several tumor-specific monoclonal antibodies. The carbohydrazide linker permits the attachment of a wide range of diagnostic and therapeutic agents provided that such agents carry, or can be made to carry, an aldehyde (or keto) group. For example, the imaging isotope 67Ga has been incorporated in place of 55Fe into the aldehyde-modified chelator used above and coupled to the F(ab)'2-like fragment of the chimeric antibody B72.3.

L23 ANSWER 36 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:531256 HCAPLUS
DOCUMENT NUMBER: 115:131256
TITLE: Attachment of linker groups to carboxyl termini using enzyme-assisted reverse proteolysis
AUTHOR(S): **Rose, Keith**; Jones, Robert M. L.; Sundaram, Ganesh; **Offord, Robin E.**
CORPORATE SOURCE: Dep. Biochim. Med., CMU, Geneva, 1211, Switz.
SOURCE: Pept., Proc. Eur. Pept. Symp., 20th (1989), Meeting Date 1988, 274-6. Editor(s): Jung, Guenther; Bayer, Ernst. de Gruyter: Berlin, Fed. Rep. Ger. CODEN: 57ACAI
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A report from a symposium on the coupling, using enzyme-catalyzed reverse proteolysis, of carbohydrazide and 1,3-diamino-2-propanol to LysB29 of des[AlaB30] insulin. Coupling yields were .apprx.70%, and electrophoresis and peptide mapping showed a single group had been attached specifically to the carboxyl group of LysB29. Oxidation of the diaminopropyl-substituted derivative with periodate gave the corresponding formylmethylamino derivative, which was conjugated to ligands carrying an aminooxy function [(aminooxyacetyl)ferrioxamine and Nα-(aminooxyacetyl)polyglutamic acid]. Coupling of the carbohydrazide deriv with 2,4-dihydroxybenzaldehyde also proceeded smoothly under similar conditions.

L23 ANSWER 37 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:427601 HCAPLUS
DOCUMENT NUMBER: 115:27601
TITLE: Reaction mechanism of trypsin-catalyzed semisynthesis of human insulin studied by fast atom bombardment mass spectrometry
AUTHOR(S): **Rose, Keith**; Stoecklin, Reto; Savoy, Luc Alain; Regamey, Pierre Olivier; **Offord, Robin**

E.; Vuagnat, Pierre; Markussen, Jan
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, 1211, Switz.
SOURCE: Protein Engineering (1991), 4(4), 409-12
CODEN: PRENE9; ISSN: 0269-2139
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The production of semisynthetic human insulin for therapeutic purposes is of considerable importance. During trypsin-catalyzed transformation of pig insulin into an ester of insulin of human sequence, the alanyl residue at position B30 is removed and replaced with an esterified residue of threonine. The authors have carried out this transformation in a medium enriched in 18OH2 and studied the product by MS. In contrast to a previous report, incorporation of label into the B29-B30 peptide bond occurred during the transformation with threonine Me ester in aqueous N,N-dimethylacetamide. Quant. data are presented and the implications of these findings are discussed.

L23 ANSWER 38 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:404606 HCAPLUS
DOCUMENT NUMBER: 115:4606
TITLE: Preparation of well-defined protein conjugates using enzyme-assisted reverse proteolysis
AUTHOR(S): **Rose, Keith**; Vilaseca, L. Antonio; Werlen, Raymond; Meunier, Anne; Fisch, Igor; Jones, Robert M. L.; **Offord, Robin E.**
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, 1211, Switz.
SOURCE: Bioconjugate Chemistry (1991), 2(3), 154-9
CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A 2-step approach to the production of well-defined protein conjugates is described. In the 1st step, a linker group, carbohydrazide, having unique reactivity (a hydrazide group) is attached specifically to the carboxyl terminus by using enzyme-catalyzed reverse proteolysis. Since the hydrazide group exists nowhere else on the protein, specificity is assured in a subsequent chemical reaction (formation of a hydrazone bond) of the modified protein with a mol. (chelator, drug, or polypeptide) carrying an aldehyde or keto group. The product is sufficiently stable at neutral pH, no reduction of the hydrazone bond being necessary for the hydrazones described. Protein modification is thus restricted to the carboxyl terminus and a homogeneous product results. With insulin as a model, conditions are described for producing such well-defined conjugates in good yields. The use of other linker groups besides carbohydrazide and applications of these techniques to antibody fragments are discussed.

L23 ANSWER 39 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:589801 HCAPLUS
DOCUMENT NUMBER: 113:189801
TITLE: Enzymic carboxyl-terminal amidation of calcitonin gene related peptide
INVENTOR(S): Carne, Alexander Fraser; **Rose, Keith**; **Offord, Robin Ewart**
PATENT ASSIGNEE(S): Celltech Ltd., UK
SOURCE: Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 375260	A1	19900627	EP 1989-313018	19891213
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
WO 9007005	A1	19900628	WO 1989-GB1490	19891213
W: GB, JP, US				
JP 03503958	T2	19910905	JP 1990-500729	19891213
GB 2236319	A1	19910403	GB 1990-16719	19900730
GB 2236319	B2	19920506		

PRIORITY APPLN. INFO.: GB 1988-29432 A 19881215
WO 1989-GB1490 W 19891213

AB Calcitonin gene-related peptide (CGRP) that has been manufactured in recombinant microorganisms is amidated at the C-terminal, to render the peptide biol. active, using an amino acid amide as substrate for a hydrolase, preferably a proteinase, in an organic solvent that may contain some water. Recombinant desphenylalanyl-amide α-CGRP 1.0 mg in water 0.04 mL was mixed with 0.2 mL of a solution of phenylalanine amide in 90% butane-1,4-diol (328.4 mg amide/2 mL diol, pH = 6.0). Thermolysin, 0.002 mL of a 50 mg/mL solution was added and the reaction incubated 22° 2 h. The reaction mixture was the fractionated by reverse-phase HPLC to recover authentic human α-CGRP with a yield of 70%.

L23 ANSWER 40 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:548404 HCAPLUS
DOCUMENT NUMBER: 113:148404
TITLE: Preparation of carboxyl-terminal hydrazide derivatives of proteins using enzyme-catalyzed reverse proteolysis
INVENTOR(S): **Offord, Robin Ewart; Rose, Keith**
PATENT ASSIGNEE(S): Switz.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9002136	A1	19900308	WO 1989-GB994	19890825
W: AU, JP, US				
EP 359428	A1	19900321	EP 1989-308681	19890825
EP 359428	B1	19950809		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AU 8941906	A1	19900323	AU 1989-41906	19890825
AU 637326	B2	19930527		
JP 03501623	T2	19910411	JP 1989-509484	19890825
JP 2778775	B2	19980723		
ES 2077582	T3	19951201	ES 1989-308681	19890825

PRIORITY APPLN. INFO.: GB 1988-20378 A 19880826
WO 1989-GB994 A 19890825

OTHER SOURCE(S): MARPAT 113:148404
AB The title derivs. AC(O)N(R1)N(R2)Z1C(X)Z2N(R3)NHR4 [I; AC(O) is a residue of protein or peptide ACO2H; R1-R4 = H, alkyl, aryl, aralkyl; Z1, Z2 = spacer group; X = O, S] and their salts are prepared The spacer group(s) may be present or absent. The protein residue in I is, e.g., an Ig residue. Enzyme-catalyzed reverse proteolysis is used to attach hydrazide groups specifically to carboxyl termini of the proteins. No side-chain protection is required and the coupling takes place under very mild

conditions in aqueous solution Thus, using porcine trypsin, IgG, and 1,1-carbonyldihydrazide, a carbonyldihydrazide derivative of IgG was prepared which corresponded in size to a F(ab')2 fragment; 0.06 mol hydrazide/mol IgG was incorporated.

L23 ANSWER 41 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:512022 HCAPLUS
DOCUMENT NUMBER: 113:112022
TITLE: Preparation of protein derivatives and their use for preparing medically useful protein conjugates
INVENTOR(S): **Offord, Robin Ewart; Rose, Keith**
PATENT ASSIGNEE(S): Switz.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9002135	A1	19900308	WO 1989-GB993		19890825
W: AU, JP, US					
AU 8942042	A1	19900323	AU 1989-42042		19890825
AU 637327	B2	19930527			
EP 360433	A1	19900328	EP 1989-308680		19890825
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
JP 03501622	T2	19910411	JP 1989-509483		19890825
PRIORITY APPLN. INFO.:			GB 1988-20377	A	19880826
			WO 1989-GB993	A	19890825

OTHER SOURCE(S): MARPAT 113:112022
AB Protein derivs. ACONR1CH2ZR2 (A = protein or peptide; R1 = H, alkyl, aryl, aralkyl; Z = spacer group, absent or present; R2 = COHR3CH2NHR4, CR3O; R3, R4 = H, alkyl, aryl, aralkyl; when A = insulin, R1 = H) and their salts are prepared by a condensation reaction catalyzed by an enzyme involving the formation of a peptide bond. The compds. may be useful for preparing protein conjugates for medical use in which a group of interest such as another protein or peptide or an effector or reporter group is coupled to the protein through a NR1CH2ZCOHR3CH2N or NR1CH2ZCH group. Thus, 1,3-diamino-2-propanol was coupled to des AlaB30 insulin (DA1) by TPCK-treated bovine trypsin and the resultant product DA1-NHCH2CHOHCH2NH2 with 70% yield was purified by HPLC and was oxidized by periodic acid to form DA1-NHCH2CHO. The aldehyde was then conjugated with aminooxyacetylferrioxamine to produce the expected orange-colored oxime derivative Unmodified zinc-free porcine insulin was not reactive with aminooxyacetylferrioxamine.

L23 ANSWER 42 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:32949 HCAPLUS
DOCUMENT NUMBER: 112:32949
TITLE: Polynucleotide hybridisation probes containing aldehyde moieties for attachment of reporter groups
INVENTOR(S): Mattson, Thomas Lee; **Offord, Robin Ewart; Rose, Keith**
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 8902475	A1	19890323	WO 1988-GB754		19880916
W: AU, JP, KR, US					
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE					
GB 2209754	A1	19890524	GB 1987-21875		19870917
AU 8823835	A1	19890417	AU 1988-23835		19880916
PRIORITY APPLN. INFO.:			GB 1987-21875	A	19870917
			WO 1988-GB754	A	19880916

AB Polynucleotides containing 5'-hydroxymethylcytosine (HMC) are glucosylated and oxidized with periodate to prepare polyaldehydic polynucleotides having aldehydic sugar residues other than on the backbone. These polyaldehydes are useful as diagnostic hybridization probes, and as a support for physiol. active substances, e.g. enzymes, monoclonal antibodies. Hybrids containing labeled polyaldehydic polynucleotide T4-HMC and T4-Bio (biotinylated T4-HMC) probes are about as stable as those formed with unmodified T4-HMC on filter paper although hybridization is less efficient with the substituted probes. In RNA-DNA hybridization, T4 polyaldehydic DNA hybridized to 32P-RNA with essentially the same efficiency (83%) as that of untreated T4 DNA.

L23 ANSWER 43 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:529878 HCAPLUS
DOCUMENT NUMBER: 111:129878
TITLE: A novel derivative of the chelon desferrioxamine for site-specific conjugation to antibodies
AUTHOR(S): Pochon, S.; Buchegger, F.; Pelegrin, A.; Mach, J. P.; **Offord, R. E.**; Ryser, J. E.; **Rose, K.**
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, 1211, Switz.
SOURCE: International Journal of Cancer (1989), 43(6), 1188-94
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The preparation is described of the modified chelator aminooxyacetylferrioxamine, and the replacement of its Fe atom by 67Ga at high specific activity. The aminooxy function of this compound was allowed to react with the aldehyde groups generated by the periodate oxidation of the oligosaccharide of a mouse IgG1 monoclonal antibody (MAb), directed against carcinoembryonic antigen (CEA). The use of the aminooxy group allowed a stable bond to be formed between the chelon and the antibody with no need for reduction Fe was removed from the ferrioxamine moiety and replaced by 67 Ga either before or after conjugation of the chelon to the antibody. In either case, the labeled antibody was injected into nude mice bearing a human colon carcinoma having the appropriate antigenicity. Unoxidized antibody, labeled with 125I by conventional methods, was coinjected as an internal control. Addnl. control expts. were carried out with a nonimmune IgG using the same 67Ga-labeled modified chelon as above. The in vivo distribution of the modified antibodies was evaluated at various times at 24-96 h after injection. The methods used were γ-camera imaging and, more quant., γ-counting of the various organs after dissection. Interestingly, with the metal-chelon-labeled antibody, the intensity and specificity of tumor labeling was comparable and, in some cases, superior to the results obtained with radioiodinated antibody. In particular, there was almost no increase in liver and spleen uptake of radioactive metal relative to radioiodine, contrary to what has been observed with most antibodies labeled with 111In after conjugation with DTPA.

L23 ANSWER 44 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:401192 HCAPLUS
DOCUMENT NUMBER: 111:1192
TITLE: The degradation of secretin by insulin proteinase
AUTHOR(S): Savoy, L. A.; Cerini, F.; Davies, J. G.; Muir, A. V.; **Rose, K.; Offord, R. E.**
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, CH 1211, Switz.
SOURCE: Colloque INSERM (1989), 174(Forum Pept., 2nd, 1988), 129-32
CODEN: CINMDE; ISSN: 0768-3154
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Insulin and glucagon were rapidly degraded by insulin proteinase, but secretin was degraded much more slowly. Tritiated insulin was degraded to the same extent in the presence or absence of secretin. Fast-atom-bombardment mass spectrometry identified the major site of cleavage of secretin as being between Gln20-Arg21.

L23 ANSWER 45 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:228179 HCAPLUS
DOCUMENT NUMBER: 110:228179
TITLE: Polypeptide and protein conjugation to proteins, reporter groups, and cytotoxic agents for diagnosis and therapy
INVENTOR(S): **Offord, Robin Ewart; Rose, Keith**
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Eur. Pat. Appl., 82 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 243929	A2	19871104	EP 1987-106113	19870428
EP 243929	A3	19891011		
EP 243929	B1	19950727		
R: CH, DE, FR, GB, IT, LI, NL				
CA 1341053	A1	20000718	CA 1987-535860	19870429
JP 62267300	A2	19871119	JP 1987-107898	19870430
JP 2528464	B2	19960828		
US 6673347	B1	20040106	US 1994-241687	19940512
JP 08259600	A2	19961008	JP 1996-46752	19960208
JP 2900992	B2	19990602		
US 2004081660	A1	20040429	US 2003-673489	20030930
PRIORITY APPLN. INFO.:			GB 1986-10551	A 19860430
			US 1987-43530	B1 19870428
			US 1988-220196	B1 19880718
			US 1989-380738	B1 19890717
			US 1990-506545	B1 19900405
			US 1991-742159	B1 19910801
			US 1992-866262	B1 19920410
			US 1993-89051	B1 19930806
			US 1994-241687	A1 19940512

OTHER SOURCE(S): MARPAT 110:228179
AB A protein is conjugated, through a coupler via Schiff base linkages which may be stabilized by reduction, to the same or another protein, a reporter

group, or a cytotoxic agent. The linkages are formed at specific sites on the protein (especially at the C-terminus by enzymic means) so as not to inactivate the active site. The reporter group may be a chelating agent which can bind a radioactive metal for use in diagnosis and therapy. The protein may be an antibody or antibody fragment. A buffered solution of m-aminobenzaldehyde di-Me acetal was added to Zn-free insulin and the mixture was incubated with trypsin to produce de-AlaB30-insulin B29-m-formylanilide. m-Aminobenzoic acid was sep. converted in 2 steps to the tert-butyloxycarbonyl-m-aminobenzoic acid hydroxysuccinimido ester, which was conjugated with ferrioxamine B and deblocked. This product was conjugated with the insulin derivative and the product was reduced with NaBH3CN. Fe was removed from the conjugate with EDTA and the conjugate was labeled with 111In or 68Ga.

L23 ANSWER 46 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:34021 HCAPLUS
DOCUMENT NUMBER: 110:34021
TITLE: Insulin proteinase liberates from glucagon a fragment known to have enhanced activity against calcium-magnesium dependent ATPase
AUTHOR(S): **Rose, Keith**; Savoy, Luc Alain; Muir, Anita V.; Davies, J. Gwynfor; **Offord, Robin E.**; Turcatti, Gerardo
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, CH-1211/4, Switz.
SOURCE: Biochemical Journal (1988), 256(3), 847-51
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Contrary to previous reports, substantial cleavage of porcine glucagon by insulin proteinase is shown to occur at only one region, namely the double-basic sequence -Arg17-Arg18-. Cleavage takes place almost exclusively between these two residues, liberating fragments glucagon-(1-17) and glucagon-(18-29). Others have shown that the fragment glucagon-(19-29) is 1000-fold more efficient, compared with intact glucagon, at inhibiting the Ca2+-activated and Mg2+-dependent ATPase activity and the Ca2+ pump of liver plasma membranes. This study shows that this fragment is not liberated in detectable quantities by the present insulin proteinase preparation On the other hand, others have shown that glucagon-(18-29), though less active than glucagon-(19-29), was still 100-fold more active than glucagon itself in the above-mentioned system. The present observations represent the first demonstration of the release by insulin proteinase of a hormone fragment having enhanced activity, although it has yet to be shown that the activity of this fragment is important in vivo. Since the formation of glucagon-(19-29) from glucagon-(18-29) would involve merely removal of Arg18, a second enzyme might exist to provide the more active fragment.

L23 ANSWER 47 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:201215 HCAPLUS
DOCUMENT NUMBER: 108:201215
TITLE: Enzyme-assisted semisynthesis of polypeptide active esters and their use
AUTHOR(S): **Rose, Keith**; Herrero, Carlos; Proudfoot, Amanda E. I.; **Offord, Robin E.**; Wallace, Carmichael J. A.
CORPORATE SOURCE: Dep. Biochim. Med., CMU, Geneva, 1211, Switz.
SOURCE: Biochemical Journal (1988), 249(1), 83-8
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal

LANGUAGE: English

AB A method is described for the preparation of polypeptides activated uniquely at the C-terminus. The polypeptide is incubated in a concentrated solution of an amino acid active ester, the latter having its amino group free but adequately protected by protonation. The amino acid ester is coupled via its amino group to the C-terminus of the polypeptide by enzymic catalysis (reverse proteolysis). The resulting polypeptide C-terminal active ester is then isolated and coupled to a suitable amino component (generally a polypeptide) in a subsequent chemical coupling. The method appears to be generally applicable; fragments of horse heart cytochrome c and porcine insulin are used as examples. Two new analogs of cytochrome c were prepared by this method, with yields of up to 60% in the final coupling. Scope and limitations of the method are discussed.

L23 ANSWER 48 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:127939 HCAPLUS
DOCUMENT NUMBER: 108:127939
TITLE: C-Terminal peptide identification by fast atom bombardment mass spectrometry
AUTHOR(S): **Rose, Keith**; Savoy, Luc Alain; Simona, Marco G.; **Offord, Robin E.**; Wingfield, Paul
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, CH-1211, Switz.
SOURCE: Biochemical Journal (1988), 250(1), 253-9
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Described is the isolation from protein digests, by reversed-phase HPLC, of 18O-labeled and unlabeled peptides and their direct anal. by fast-atom-bombardment mass spectrometry. Under the conditions used, the 18O label is retained throughout the separation and anal., thus permitting assignments of C-terminal peptides to be made. Enzyme-catalyzed exchange of label into the terminal carboxy group occurred in some cases without hydrolysis of a peptide bond. This effect, which may be exploited to prepare labeled peptides, does not prevent application of the method (2 sep. digests must then be used). The method was used for the anal. of enzymic partial hydrolyzates of glucagon, insulin, and of several proteins produced by expression of recombinant DNA.

L23 ANSWER 49 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:75830 HCAPLUS
DOCUMENT NUMBER: 108:75830
TITLE: Enzyme-assisted semisynthesis of polypeptide active esters for subsequent spontaneous coupling
AUTHOR(S): **Rose, Keith**; Herrero, Carlos; Proudfoot, Amanda E. I.; Wallace, Carmichael J. A.; **Offord, Robin E.**
CORPORATE SOURCE: Dep. Biochim. Med., CMU, Geneva, 1211, Switz.
SOURCE: Pept., Proc. Eur. Pept. Symp., 19th (1987), Meeting Date 1986, 219-22. Editor(s): Theodoropoulos, Dimitrios. de Gruyter: Berlin, Fed. Rep. Ger.
CODEN: 56ABA8
DOCUMENT TYPE: Conference
LANGUAGE: English

AB A symposium. Several methods are given for achieving enzyme-assisted specific carboxyl-terminal activation.

L23 ANSWER 50 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:73676 HCAPLUS
DOCUMENT NUMBER: 108:73676

TITLE: Enzymic semisynthesis of insulin specifically labeled with tritium at position B-30
AUTHOR(S): Davies, J. Gwynfor; **Rose, Keith**; Bradshaw, Charles G.; **Offord, Robin E.**
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, CH-1211, Switz.
SOURCE: Protein Engineering (1987), 1(5), 407-11
CODEN: PRENE9; ISSN: 0269-2139
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Porcine insulin labeled with 3H at position 30 of the B chain was prepared by using Achromobacter lyticus protease to couple L-[3H]alanine Me ester to Des-AlaB30-porcine insulin followed by hydrolysis of the Me ester. By this methodol., 1 nM insulin would give .apprx.2000 disintegrations/min with [3H]alanine at 2 Ci/mmol. Results obtained by using carboxypeptidase Y and bovine and porcine trypsin are briefly discussed.

L23 ANSWER 51 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:49719 HCAPLUS
DOCUMENT NUMBER: 108:49719
TITLE: Identification by fast atom bombardment mass spectrometry of insulin fragments produced by insulin proteinase
AUTHOR(S): Savoy, Luc Alain; Jones, Robert M. L.; Pochon, Sibylle; Davies, J. Gwynfor; Muir, Anita V.; **Offord, Robin E.; Rose, Keith**
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, CH-1211, Switz.
SOURCE: Biochemical Journal (1988), 249(1), 215-22
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The isolation by reversed-phase HPLC of a number of products of the degradation of insulin by insulin proteinase and their direct anal. by fast-atom bombardment mass spectrometry (f.a.b.-m.s.) is described. Various semisynthetically labeled insulins were used, including [[2H2]GlyA1]insulin and [[18O]LysB29]insulin. The results obtained confirm and extend the results obtained by non-mass-spectrometric methods. Cleavage sites were identified between positions A13-A14, A14-A15, B9-B10, B13-B14, B24-B25, and B25-B26. The advantages and disadvantages of the application of f.a.b.-m.s. to such studies are discussed.

L23 ANSWER 52 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:49718 HCAPLUS
DOCUMENT NUMBER: 108:49718
TITLE: Identification of radioactive insulin fragments liberated by insulin proteinase during the degradation of semisynthetic [[3H]GlyA1]insulin and [[3H]PheB1]insulin
AUTHOR(S): Davies, J. Gwynfor; Muir, Anita V.; **Rose, Keith; Offord, Robin E.**
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, CH-1211, Switz.
SOURCE: Biochemical Journal (1988), 249(1), 209-14
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 3H-labeled porcine insulin was cleaved by insulin proteinase from rat muscle between TyrA14-GlnA15, GluB13-AlaB14, and HisB10-LeuB11 as determined by HPLC and paper electrophoresis.

L23 ANSWER 53 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:38412 HCAPLUS
DOCUMENT NUMBER: 108:38412
TITLE: Semisynthetic human [[3H2]Phe1]proinsulin
AUTHOR(S): Jones, Robert M. L.; **Rose, Keith**; **Offord, Robin E.**
CORPORATE SOURCE: Dep. Biochem. Med., Cent. Med. Univ., Geneva, 1211/4, Switz.
SOURCE: Biochemical Journal (1987), 247(3), 785-8
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Biosynthetic human proinsulin (obtained by recombinant DNA techniques) was used as the starting material for the preparation, by semisynthetic methods, of [3H]proinsulin with the label at the N-terminal phenylalanine residue. The labeled proinsulin was characterized by its retention time on reversed-phase HPLC, PAGE, the time course of its enzymic conversion into insulin, and chromatog. anal. after extensive proteolytic degradation The specific radioactivity of the product was 5 Ci/mmol.

L23 ANSWER 54 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:571918 HCAPLUS
DOCUMENT NUMBER: 107:171918
TITLE: The state of the N-terminus of recombinant proteins: determination of N-terminal methionine (formylated, acetylated, or free)
AUTHOR(S): **Rose, Keith**; Savoy, Luc Alain; Simona, Marco G.; **Offord, Robin E.**; Wingfield, Paul T.; Mattaliano, Robert J.; Thatcher, David R.
CORPORATE SOURCE: Dep. Biochim. Med., CMU, Geneva, 1211/4, Switz.
SOURCE: Analytical Biochemistry (1987), 165(1), 59-69
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The removal of N-terminal methionine from proteins produced by recombinant DNA techniques is often far from quant. Furthermore, a proportion of the methionylated product may be Nα-flocked and thus not easily accessible to conventional (Edman) techniques of protein characterization. In this paper, a method for overcoming the resulting anal. problems is described. The techniques based on perdeuteroacetylation (performed only if unblocked methionine is to be determined), cleavage with CNBr, extraction of any acylhomoserine lactone into EtOAc formation of a chemical derivative, and anal. by combined gas chromatog./mass spectrometry (GC/MS). The remaining fragments, insol. in CNBr are available for further anal. by mass spectrometric or other methods if required. Using an acylhomoserine lactone labeled with a stable isotope as internal standard,the method is semiquant. It should be possible to develop a quant. method if appropriate polypeptide stds. are prepared N-Terminal processing of 8 recombinant proteins is discussed.

L23 ANSWER 55 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:530420 HCAPLUS
DOCUMENT NUMBER: 107:130420
TITLE: Press-stud protein conjugates
AUTHOR(S): **Offord, R. E.**; Pochon, S.; **Rose, K.**
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, 1211, Switz.
SOURCE: Pept., Proc. Eur. Pept. Symp., 19th (1987), Meeting

Date 1986, 279-81. Editor(s): Theodoropoulos, Dimitrios. de Gruyter: Berlin, Fed. Rep. Ger.
CODEN: 56ABA8
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A method for the preparation of protein conjugates that preserves the behavior of unsubstituted protein while affording maximal labeling is discussed. The press-stud coupling technique, involving the fastening of complementary side-chains, is discussed as a method to achieve this goal.

L23 ANSWER 56 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:98595 HCAPLUS
DOCUMENT NUMBER: 106:98595
TITLE: Press-stud protein conjugates
AUTHOR(S): **Offord, R. E.; Rose, K.**
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, CH-1211/4, Switz.
SOURCE: Protides of the Biological Fluids (1986), 34, 35-8
CODEN: PBFPA6; ISSN: 0079-7065
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Protein conjugation restricted to 1 or a few sites fastened only to complementary partners (press-stud principle used on clothing) is described and an example of insulin conjugation is presented. Application of the method in labeling target-seeking proteins, such as monoclonal antibodies and Fab fragments of IgG, is described for imaging in vivo. The label can be radioactive for scintigraphy or paramagnetic for NMR.

L23 ANSWER 57 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:432376 HCAPLUS
DOCUMENT NUMBER: 103:32376
TITLE: Oxygen-18 labeled human insulin: semisynthesis and mass-spectrometric analysis
AUTHOR(S): **Rose, Keith**; Pochon, Sibylle; **Offord, Robin**
CORPORATE SOURCE: Dep. Biochim. Med., Univ. Geneve, Geneva, CH-1211, Switz.
SOURCE: Pept., Proc. Eur. Pept. Symp., 18th (1984), 235-8. Editor(s): Ragnarsson, Ulf. Almqvist & Wiksell: Stockholm, Swed.
CODEN: 53PWAN
DOCUMENT TYPE: Conference
LANGUAGE: English
AB 18O-labeled human insulin [9004-10-8] was prepared by the method of K. Rose et al. (1984) except that the porcine insulin and trypsin were freeze-dried from H218O before starting. The product was characterized by a variety of methods and the protease of Amillaria melles gave as its sole products the peptide Lys-Thr (residues B29-30) and the remainder of the mol. Gas-liquid chromatog. and mass spectrum anal. established that 18O was incorporated into the carbonyl group of lysine-B29. The isotope abundance was approx. 85 atom percent, higher than the 75 atom percent previously reported. This isotopic abundance is apparently sufficient for detecting the compound at physiol. or sub-physiol. levels; as little as 1-5 pmoles can probably be detected.

L23 ANSWER 58 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:468902 HCAPLUS
DOCUMENT NUMBER: 101:68902
TITLE: A case of spurious product formation during attempted resynthesis of proteins by reverse proteolysis. Some

batches of 'pure' glycerol contain crosslinking agents
AUTHOR(S): Proudfoot, Amanda E. I.; **Offord, Robin E.**; **Rose, Keith**; Schmidt, Maurice; Wallace, Carmichael J. A.
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, 1211/4, Switz.
SOURCE: Biochemical Journal (1984), 221(2), 325-31
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In cases where enzyme-catalyzed synthesis of a peptide bond is being used to reform a protein from 2 large peptide fragments, the organic cosolvent chosen has so far been glycerol, for most solvents in use in small-mol. systems are potent protein denaturants. However, impurities contaminating certain batches of glycerol are effective in crosslinking the complexes formed by these peptide fragments, thus mimicking the enzyme-catalyzed process. In 1 such case, the reported reformation of cytochrome c from a 2-fragment complex system, cytochrome c-T, the extent and rate of conjugate formation duplicates that reported for enzymic resynthesis. No difference was observed between mixts. containing or lacking enzyme. The danger of confusion possible to those engaged in studies of resynthesis is mentioned, and a simple control of purchased glycerol to avoid the problem is suggested. Similar caution is recommended to those (x-ray crystallographers and others) who seek to stabilize protein solns. by adding large quantities of glycerol.

L23 ANSWER 59 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:438818 HCAPLUS
DOCUMENT NUMBER: 101:38818
TITLE: A mass-spectrometric investigation of the mechanism of the semisynthetic transformation of pig insulin into an ester of insulin of human sequence
AUTHOR(S): **Rose, Keith**; Gladstone, James; **Offord, Robin E.**
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, 1211/4, Switz.
SOURCE: Biochemical Journal (1984), 220(1), 189-96
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the trypsin-mediated semisynthetic transformation of pig insulin into an ester of insulin of human sequence, the B30 alanine residue of the pig hormone is replaced by an ester of threonine. The mechanism of this reaction was investigated by carrying out the transformation in a medium containing water enriched with 18O. Subsequent anal. by combined gas-liquid chromatog.-mass spectrometry demonstrated that the oxygen isotope is incorporated into the B29 carbonyl group of the insulin ester product. The transformation occurs in the above system by a mechanism involving hydrolysis followed by coupling and not by direct transpeptidation as has been previously found for another system.

L23 ANSWER 60 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:4461 HCAPLUS
DOCUMENT NUMBER: 100:4461
TITLE: A new mass-spectrometric C-terminal sequencing technique finds a similarity between γ-interferon and α2-interferon and identifies a proteolytically clipped γ-interferon that retains full antiviral

activity
AUTHOR(S): **Rose, Keith**; Simona, Marco G.; **Offord, Robin E.**; Prior, Christopher P.; Otto, Berndt; Thatcher, David R.
CORPORATE SOURCE: Dep. Biochim., Cent. Med. Univ., Geneva, 1211/4, Switz.
SOURCE: Biochemical Journal (1983), 215(2), 273-7
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB During peptide sequence mapping, it is difficult to obtain sequence information from the C-terminus ; it is much easier to obtain sequence information from the N-terminus of a protein (Rose, K., et al, 1983). A novel mass-spectrometric technique is described here which permits identification of the C-terminal peptide of a protein. This technique involves the incorporation of 18O into all α-carboxy groups liberated during enzyme-catalyzed partial hydrolysis of the protein, followed by mass spectrometry to identify as the C-terminal peptide the only peptide that did not incorporate any 18O. This technique was used to identify the true C-terminal tryptic peptide of a bacterially-produced (recombinant technol.) γ-interferon (human) and to distinguish it from a peptide produced by an anomalous tryptic cleavage. A closely similar sequence segment of bacterially produced α2-interferon undergoes an analogous cleavage. The C-terminus of a clipped γ-interferon that retains full antiviral activity also was identified by using the technique.

L23 ANSWER 61 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:2927 HCAPLUS
DOCUMENT NUMBER: 100:2927
TITLE: Amino acid sequence determination by gas chromatography-mass spectrometry of permethylated peptides. The application of capillary columns
AUTHOR(S): **Rose, Keith**; Bairoch, Amos; **Offord, Robin E.**
CORPORATE SOURCE: Dep. Biochim. Med., CMU, Geneva, 1211, Switz.
SOURCE: Journal of Chromatography (1983), 268(2), 197-206
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The application of capillary columns to the determination of the amino acid sequence of proteins and polypeptides by gas chromatog.-mass spectrometry (GC-MS) of partial hydrolyzates is described and discussed for the case of the Nα,ε-trifluoroacetyl-N,O-permethyl derivs. Retention indexes are determined with the aid of a computer program. The mass spectra of methionine enkephalin obtained by GC-MS on a packed and on a capillary column are presented and a retention index calculated Amts. of derivative corresponding to subnanomole amts. of peptides are sufficient to provide full amino acid sequence information. To assist in the assignment of retention indexes above 4400, a mixture of n-alkanes from a com. source was characterized by GC-MS up to n-C54H110, and was found to contain material up to an expected C72H146.

L23 ANSWER 62 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:609213 HCAPLUS
DOCUMENT NUMBER: 99:209213
TITLE: Amino acid sequence determination by GLC-mass spectrometry of permethylated peptides. Optimization of the formation of chemical derivatives at the 2-10-nmol level

AUTHOR(S): **Rose, Keith**; Simona, Marco G.; **Offord, Robin E.**
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, 1211/4, Switz.
SOURCE: Biochemical Journal (1983), 215(2), 261-72
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new technique is described that permits the permethylation of acylated peptides at the 2-10-nmol level. The presence of up to 400 μg SDS per sample does not affect the reaction yields. The technique, which is a miniaturization of the widely used MeI/dimethylsulfinyl carbanion procedure, employs a layer of hexane to exclude moisture and O from the reaction mixture Anal. of the peptide derivs. by combined gas chromatog. (GLC)-mass spectrometry permits amino acid sequence information to be obtained. In addition to studies of digests of a model substrate (glucagon), the new permethylation technique was used to identify a peptide of interest from a digest of a cytochrome and to define the N-termini of 2 proteins at the 5-nmol level.

L23 ANSWER 63 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:593177 HCAPLUS
DOCUMENT NUMBER: 99:193177
TITLE: Human insulin from non-human insulin
INVENTOR(S): **Offord, Robin Ewart; Rose, Keith**
PATENT ASSIGNEE(S): Switz.
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8302772	A1	19830818	WO 1983-GB34	19830207
W: JP				
EP 87238	A1	19830831	EP 1983-300603	19830207
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				

PRIORITY APPLN. INFO.: GB 1982-3526 A 19820208
GB 1982-32809 A 19821117

AB Porcine insulin [12584-58-6] or a des-insulin is converted to human insulin [11061-68-0] by trypsin [9002-07-7] in a nonaq. solvent. Thus, 62.3 mg L-threonine-O-tert-Bu ether-tert-Bu ester [5854-78-4] was mixed with 20 mg porcine insulin suspended in 660 mg of a solution composed of 2 vols. 1,4-butanediol [110-63-4] and 1 volume of a 1.5M Tris-HCl solution in DMSO. Then, 30 μL of a solution of L-1-tosylamide-2-phenylethyl chloromethyl ketone-inhibited trypsin was added. After stirring for 1 h at 37°, the reaction was stopped by chilling and addition of glacial HOAc. The reaction product was isolated by dilution and gel filtration. The yield was 20.1 mg, 99% of theor. The B30 threonine residue was deprotected by dissolving the freeze-dried product in 2 mL CF3COOH containing 1 mg tryptophan and holding at 22° for 45 min. The yield of human insulin was 18.5 mg, 93% of theor.

L23 ANSWER 64 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:571579 HCAPLUS
DOCUMENT NUMBER: 99:171579
TITLE: Evidence for the vitamin K-dependent γ-carboxylation of the first glutamic acid

residue in peptide substrates containing a diglutamyl sequence
AUTHOR(S): Burgess, Annette I.; Esnouf, M. Peter; **Rose, Keith**; **Offord, Robin E.**
CORPORATE SOURCE: Nuffield Dep. Clin. Biochem., Univ. Oxford, Oxford, OX2 6HE, UK
SOURCE: Biochemical Journal (1983), 215(1), 75-81
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The peptide substrate commonly used in vitamin K-dependent carboxylation, Phe-Leu-Glu-Glu-Val, was shown, by the use of high-voltage paper electrophoresis, to be degraded from the N-terminus by a microsomal leucine aminopeptidase. The replacement of phenylalanine with a N-tert-butoxycarbonyl group resulted in a tetrapeptide substrate with a blocked N-terminus resistant to enzymic degradation Vitamin K-dependent carboxylation of this nondegradable substrate gave a unique carboxylated product, which was separated from microsomal protein and unchanged substrate by using DEAE-Sephadex A25 as a final step. The carboxylated product was subsequently decarboxylated in 2HCl and analyzed by using GLC coupling to a mass spectrometer. This showed that only the 1st glutamic acid residue in the peptide substrate was carboxylated.

L23 ANSWER 65 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:522892 HCAPLUS
DOCUMENT NUMBER: 99:122892
TITLE: Rapid preparation of human insulin and insulin analogs in high yield by enzyme-assisted semisynthesis
AUTHOR(S): **Rose, Keith**; De Pury, Helen; **Offord, Robin E.**
CORPORATE SOURCE: Dep. Biochim. Med., Cent. Med. Univ., Geneva, 1211/4, Switz.
SOURCE: Biochemical Journal (1983), 211(3), 671-6
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Reaction conditions are described that permit the enzyme-assisted semi synthetic replacement of residue B30 of pig insulin (or of an analog) to proceed in very high yield in 2 h or less. Immobilized trypsin may be used as catalyst, and excess amino acid ester may be recycled after a simple extraction Alanine-B30 may be replaced by a variety of nucleophiles, including threonine O-tert-Bu ether tert-Bu ester, in which case the yield of crude product is about 99%. Deprotection of the B30 threonyl ester analog of insulin thus formed then affords human insulin in an overall yield of about 92%, based on pig starting material. The product has full biol. potency, as determined by depression of blood glucose concentration in rats, and showed the expected behavior on radioimmunoassay.

L23 ANSWER 66 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:501780 HCAPLUS
DOCUMENT NUMBER: 99:101780
TITLE: Development of a gas chromatography-mass spectrometry assay for the two eosinophil chemotactic factors of anaphylaxis
AUTHOR(S): Mallet, A. I.; **Rose, K.**; Priddle, J. D.
CORPORATE SOURCE: Inst. Dermatol., London, E9 6BX, UK
SOURCE: Biomedical Mass Spectrometry (1983), 10(3), 120-5
CODEN: BMSYAL; ISSN: 0306-042X
DOCUMENT TYPE: Journal

LANGUAGE: English

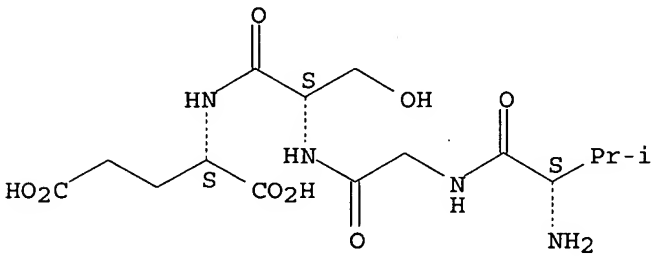
AB A capillary gas chromatog.-electron impact mass spectrometric assay was developed for Val-Gly-Ser-Glu and Ala-Gly-Ser-Glu, which have a role in the inflammatory process in skin disorders. The peptides were extracted from plasma and derivatized as trifluoroacetyl, permethyl, and trimethylsilyl derivs.

IT **61756-22-7 61756-28-3**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood plasma of humans by gas chromatog.-mass spectroscopy)

RN 61756-22-7 HCAPLUS

CN L-Glutamic acid, L-valylglycyl-L-seryl- (9CI) (CA INDEX NAME)

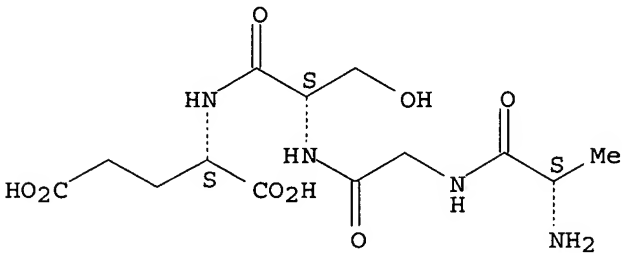
Absolute stereochemistry.



RN 61756-28-3 HCAPLUS

CN L-Glutamic acid, L-alanylglycyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

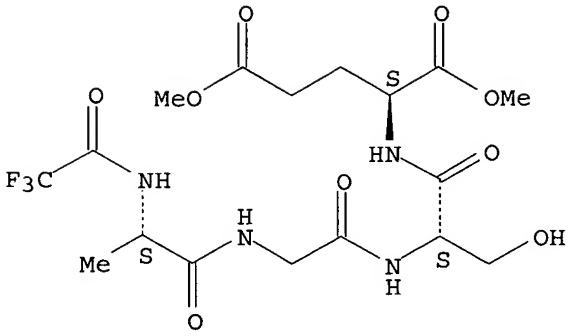


IT **86860-43-7 86860-44-8 86860-45-9 86860-46-0**
RL: PRP (Properties)
(mass spectrum of)

RN 86860-43-7 HCAPLUS

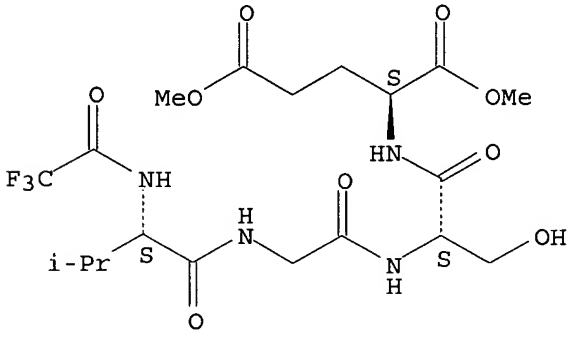
CN L-Glutamic acid, N-[N-[N-[N-(trifluoroacetyl)-L-alanyl]glycyl]-L-seryl]-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



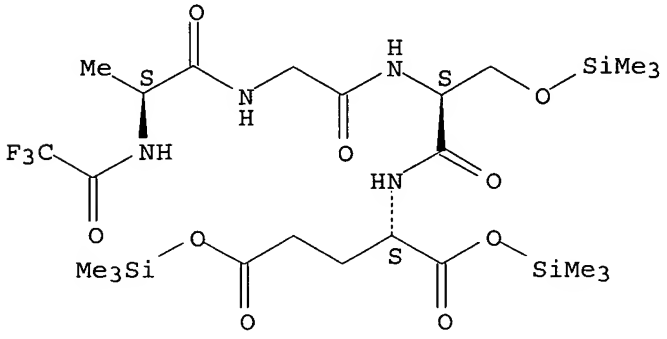
RN 86860-44-8 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N-(trifluoroacetyl)-L-valyl]glycyl]-L-seryl]-, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



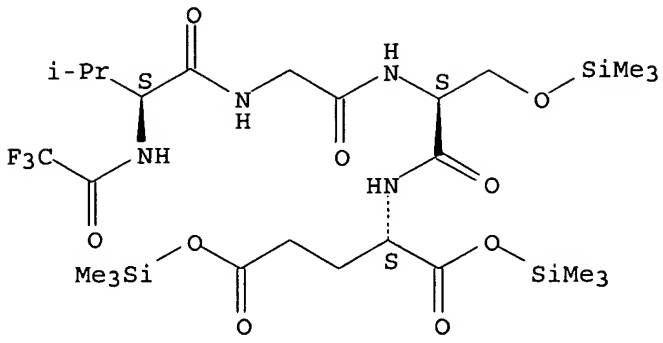
RN 86860-45-9 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N-(trifluoroacetyl)-L-alanyl]glycyl]-O-(trimethylsilyl)-L-seryl]-, bis(trimethylsilyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 86860-46-0 HCAPLUS
CN L-Glutamic acid, N-[N-[N-[N-(trifluoroacetyl)-L-valyl]glycyl]-O-(trimethylsilyl)-L-seryl]-, bis(trimethylsilyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



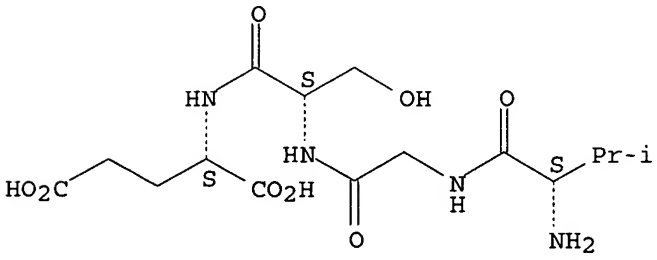
L23 ANSWER 67 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:415835 HCAPLUS
DOCUMENT NUMBER: 99:15835
TITLE: Simple and effective direct coupling for gas chromatography-mass spectrometry on the MS 50 mass spectrometer. Full spectra up to n-tetrapentacontane
AUTHOR(S): **Rose, Keith**
CORPORATE SOURCE: Dep. Biochim. Med., Geneva, 1211/4, Switz.
SOURCE: Journal of Chromatography (1983), 259(3), 445-52
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A very simple, convenient, and inexpensive interface is described which permits the insertion of fused-silica capillary tubing directly into the ion source of the MS 50 mass spectrometer. The design preserves the convenience of a vacuum-loaded reentrant, and the only ferrules used are easily accessible inside the oven of the gas chromatograph. Results with the new interface are superior to those obtained with the com. interface. The tetrapeptide Val-Gly-Ser-Glu, as its Nα-trifluoroacetyl-N,O-permethyl derivative, is used as an example. Under appropriate gas chromatog. conditions, alkanes up to n-C54H110 can be eluted and give spectra up to the mol. ion.

IT **61756-22-7**
RL: PRP (Properties); ANST (Analytical study)
(gas chromatog.-mass spectrometry of, as Nα-trifluoroacetyl-N,O-permethyl derivs.)

RN 61756-22-7 HCAPLUS
CN L-Glutamic acid, L-valylglycyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L23 ANSWER 68 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:512359 HCAPLUS
DOCUMENT NUMBER: 95:112359
TITLE: The role of the arginine-B22 residue in insulin action
AUTHOR(S): **Rose, Keith**; Rees, Anthony R.; Drake, Christopher S.; **Offord, Robin E.**
CORPORATE SOURCE: Dep. Zool., Univ. Oxford, Oxford, OX1 3PS, UK
SOURCE: Biochemical Journal (1981), 195(3), 765-8
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The side chain of the arginine-B22 residue of insulin was modified by the N8,N9-(1,2-dihydroxycyclohex-1,2-ylene) group and by the adipoyl group; these are the first insulin derivs. described that contained a modified arginine residue in an otherwise unaltered mol. When tested for their ability to lower blood sugar concentration, both modified insulins showed the same sp. activity as that of insulin. Since the substituent groups involved are very bulky and one is of opposite charge to that of the side chain, the retention of biol. activity casts doubt on the idea that the arginine-B22 residue is essential to that activity.

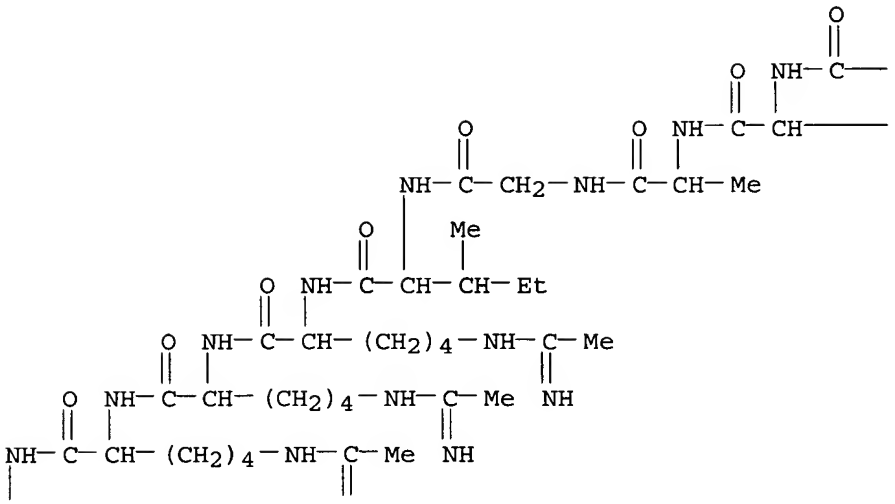
L23 ANSWER 69 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:457388 HCAPLUS
DOCUMENT NUMBER: 95:57388
TITLE: Affinity technique for the isolation of polypeptides containing arginine modified with cyclohexane-1,2-dione, and their analysis by combined gas-liquid chromatography-mass spectrometry
AUTHOR(S): **Rose, Keith**; Priddle, John D.; **Offord, Robin E.**
CORPORATE SOURCE: Lab. Mol. Biophys., Dep. Zool., Oxford, OX1 3PS, UK
SOURCE: Journal of Chromatography (1981), 210(2), 301-9
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A technique is described whereby a polypeptide containing an arginine residue that has been modified with cyclohexane-1,2-dione may be digested with a protease and any arginine-containing peptides specifically adsorbed to an affinity column consisting of immobilized borate. After desorption, the peptides may be converted into a derivative compatible with N-trifluoroacetylation and permethylation and then subjected to anal. by gas chromatog.-mass spectrometry. Alternatively, after isolation the cyclohexanedione group may be removed and the peptide analyzed by conventional procedures. Improved reaction conditions, involving use of urea, for modification with cyclohexanedione are described that were used successfully to modify insulin and a 65-residue heme-containing fragment from cytochrome c. The sequence Arg-Gly-Phe was identified by mass spectrometry in a peptide isolated by affinity chromatog. of a digest of cyclohexanedione-modified insulin. The methods are appropriate both to primary structure determination and in structure-function studies via chemical modification of arginine residues.

L23 ANSWER 70 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1980:440783 HCAPLUS
DOCUMENT NUMBER: 93:40783
TITLE: A mass-spectrometric method for the estimation of the ratio of γ-carboxyglutamic acid to glutamic acid at specific sites in proteins: application to the N-terminal region of bovine prothrombin

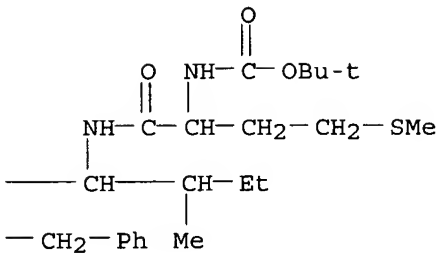
AUTHOR(S): **Rose, Keith**; Priddle, John D.; **Offord, Robin E.**; Esnouf, M. Peter
CORPORATE SOURCE: Dep. Zool., Univ. Oxford, Oxford, OX1 3PS, UK
SOURCE: Biochemical Journal (1980), 187(1), 239-43
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Decarboxylation of a polypeptide (the N-terminal region of bovine prothrombin) containing γ-carboxyglutamic acid in 2H2O resulted in formation of glutamic-γ,γ-2H2. Proteolytic digestion produced peptides containing 2H2-substituted and unsubstituted glutamic acid residues in the original carboxyglutamate:glutamate ratio. This ratio was determined by gas chromatog.-mass spectrometry of the peptides. Thus, the degree of glutamate γ-carboxylation in particular positions of the peptide could be determined

L23 ANSWER 71 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:204487 HCAPLUS
DOCUMENT NUMBER: 90:204487
TITLE: Semisynthetic analogs of cytochrome c: modification to fragment (66-104)
AUTHOR(S): Wallace, C. J. A.
CORPORATE SOURCE: Dep. Zool., Univ. Oxford, Oxford, UK
SOURCE: Semisynth. Pept. Proteins, Pap. Int. Meet. Protein Semisynth. (1978), Meeting Date 1977, 101-14.
Editor(s): **Offord, R. E.; Di Bello, C.**
Academic: London, Engl.
CODEN: 39MMAW
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Cytochrome c was Nε-acetimidated and then cleaved with BrCN to give fragment A (1-65), fragment B (66-80) [R-Glu(OR1)-Tyr-Leu-Glu(OR1)-Asn-Pro-Lys(A)-Lys(A)-Tyr-Ile-Pro-Gly-Thr-X-R2 [I; R = R1 = H, A = acetimidoyl, X = Lys(A), R2 = homoserine lactone] (II), and fragment C (81-104). II was esterified with MeOH and treated with BOCN3 (BOC = Me3CO2C) to give I [R = BOC, R1 = Me, X = Lys(A), R2 = homoserine lactone], which underwent lactone cleavage to give the corresponding I (R2 = homoserine residue). The latter was cleaved with carboxypeptidase A to give I (R, R1, X = same; R2 = OH) (B-1), which was cleaved with carboxypeptidase B to give I [R, R1 = same; X = bond; R2 = OH (B-2)]. Fragment C was coupled with BOC-Met-OSu (Su = succinimido) and BOC-deblocked to give methionyl-C. Methionyl-[Phe(F-4)82]-C was also prepared The fragment C analogs were coupled with B-1 or B-2 to give the corresponding semisynthetic BC fragments; [Asp66, Phe(F-4)82]-BC was also prepared The BC fragments were BOC-deblocked and saponified to give deprotected BC fragments, which can be coupled to fragment A to give semisynthetic cyctochrome c analogs.
IT **70291-13-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deblocking of)
RN 70291-13-3 HCAPLUS
CN L-Glutamic acid, N-[(1,1-dimethylethoxy)carbonyl]-L-methionyl-L-isoleucyl-L-phenylalanyl-L-alanylglycyl-L-isoleucyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-L-threonyl-L-α-glutamyl-L-arginyl-L-α-glutamyl-L-α-aspartyl-L-leucyl-L-isoleucyl-L-alanyl-L-tyrosyl-L-leucyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-L-alanyl-L-threonyl-L-asparaginyl- (9CI) (CA INDEX NAME)

PAGE 1-B



PAGE 1-C



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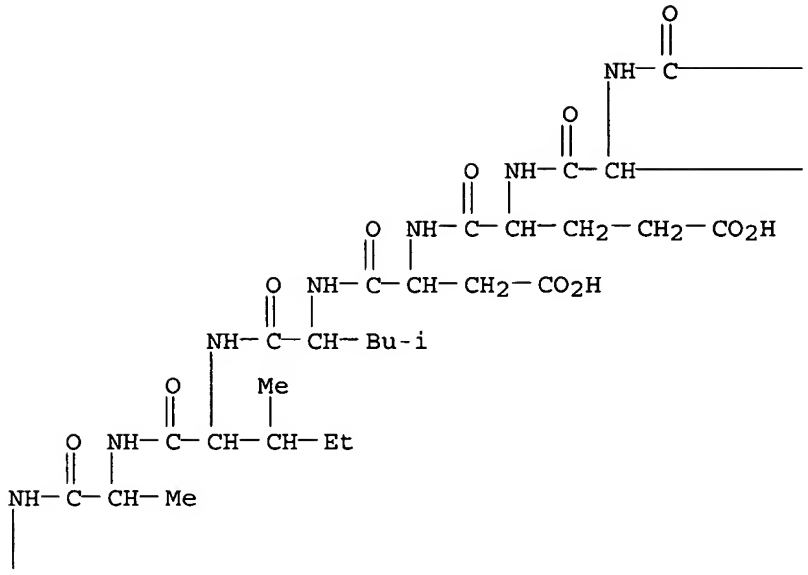

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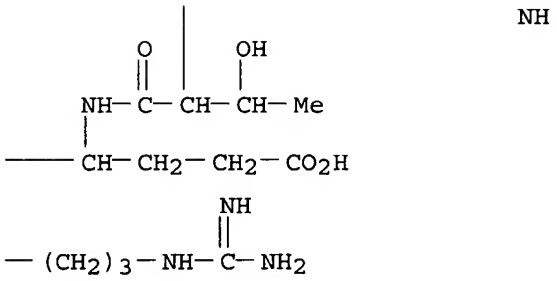

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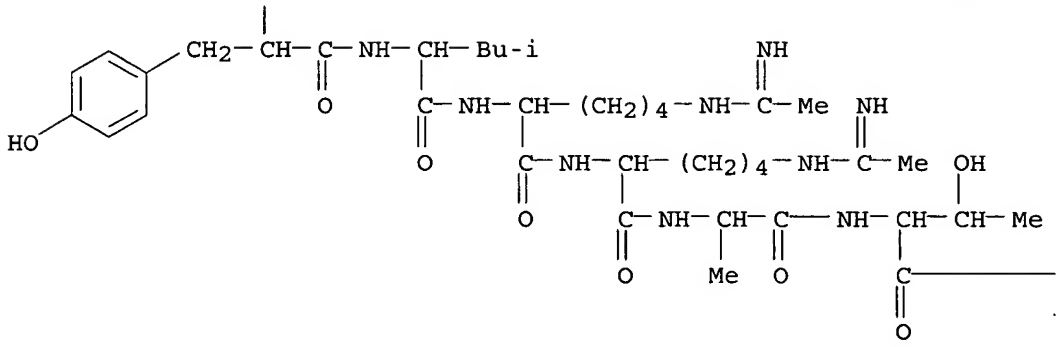

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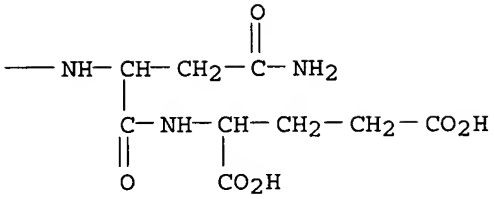
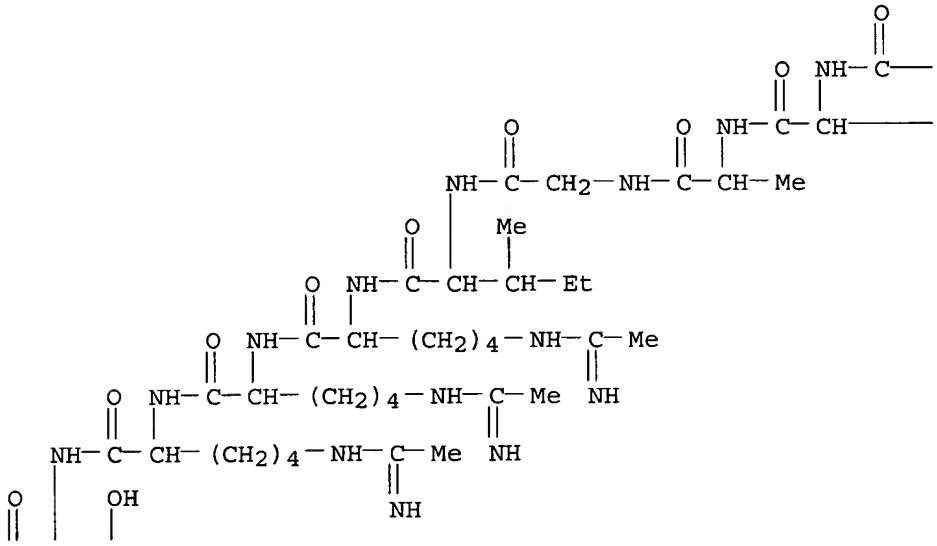


IT **70291-14-4P 70291-15-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with cyctochrome c fragments)
RN 70291-14-4 HCAPLUS
CN L-Glutamic acid, L-methionyl-L-isoleucyl-L-phenylalanyl-L-alanylglycyl-L-isoleucyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-L-threonyl-L-α-glutamyl-L-arginyl-L-α-glutamyl-L-α-aspartyl-L-leucyl-L-isoleucyl-L-alanyl-L-tyrosyl-L-leucyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-L-alanyl-L-threonyl-L-asparaginyl- (9CI) (CA INDEX NAME)

PAGE 1-B



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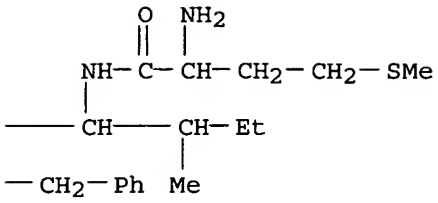

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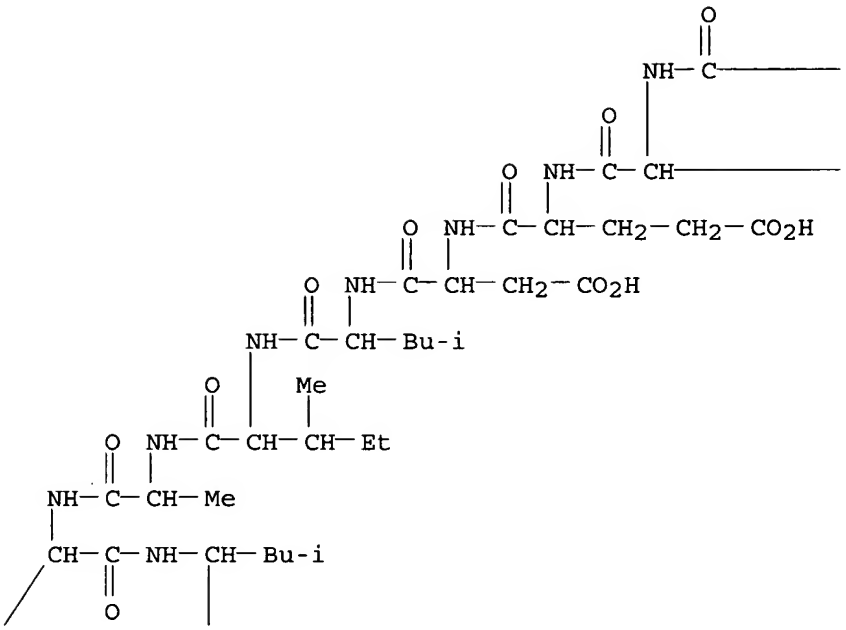

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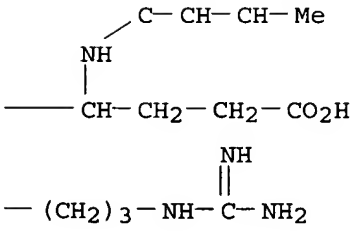

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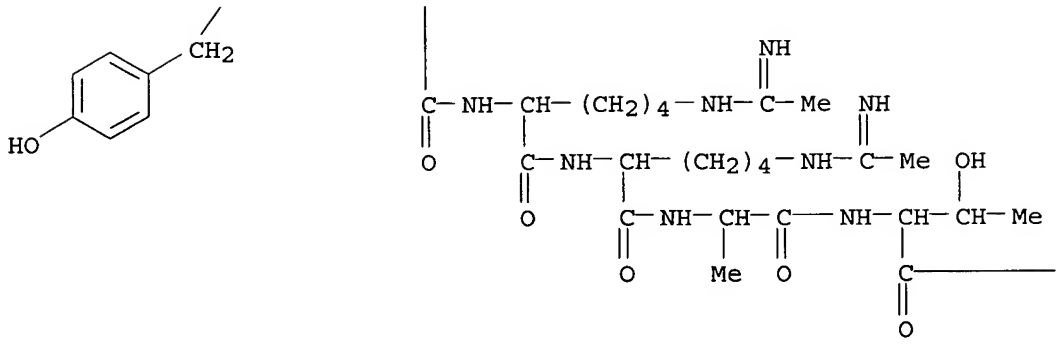

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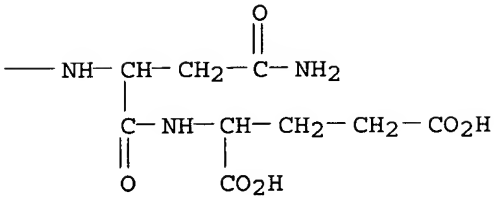
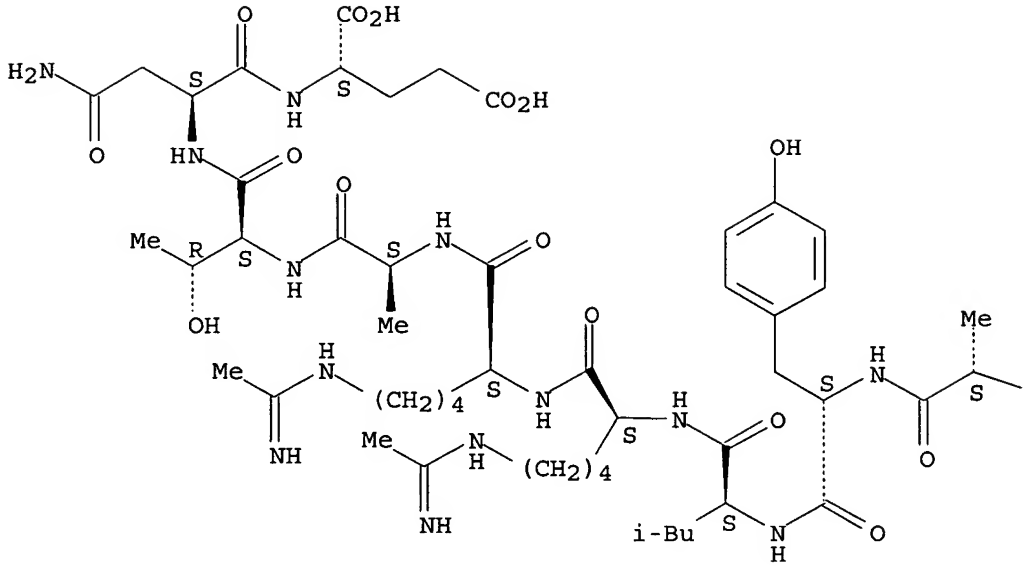


RN 70291-15-5 HCAPLUS
CN L-Glutamic acid, L-methionyl-L-isoleucyl-2-fluoro-L-phenylalanyl-L-alanylglycyl-L-isoleucyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-L-threonyl-L-α-glutamyl-L-arginyl-L-α-glutamyl-L-α-aspartyl-L-leucyl-L-isoleucyl-L-alanyl-L-tyrosyl-L-leucyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-L-alanyl-L-threonyl-L-asparaginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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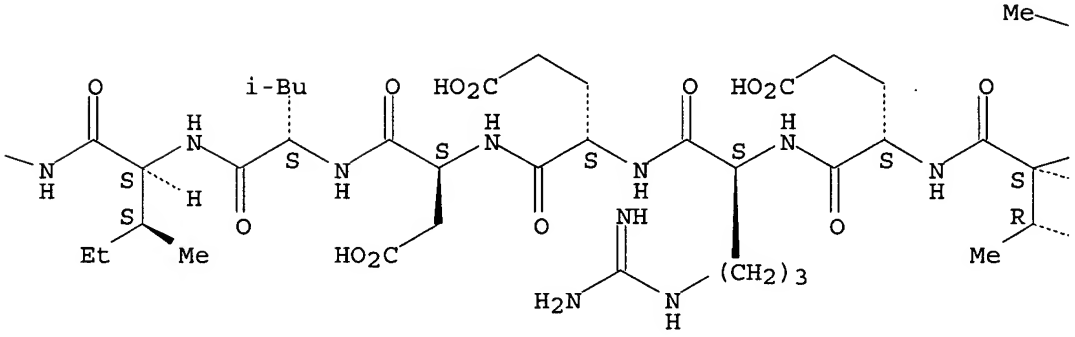

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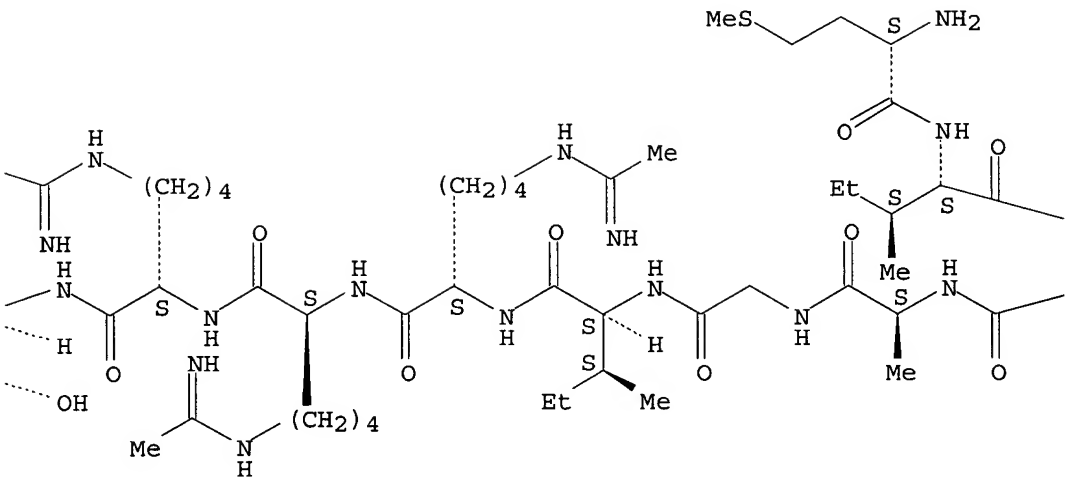
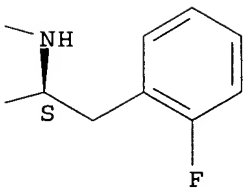


PAGE 1-D

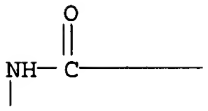


IT **70291-12-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with methionine derivative)

RN 70291-12-2 HCAPLUS

CN L-Glutamic acid, L-isoleucyl-L-phenylalanyl-L-alanylglycyl-L-isoleucyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-L-threonyl-L-α-glutamyl-L-arginyl-L-α-glutamyl-L-α-aspartyl-L-leucyl-L-isoleucyl-L-alanyl-L-tyrosyl-L-leucyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-L-alanyl-L-threonyl-L-asparaginyl- (9CI) (CA INDEX NAME)

PAGE 1-A



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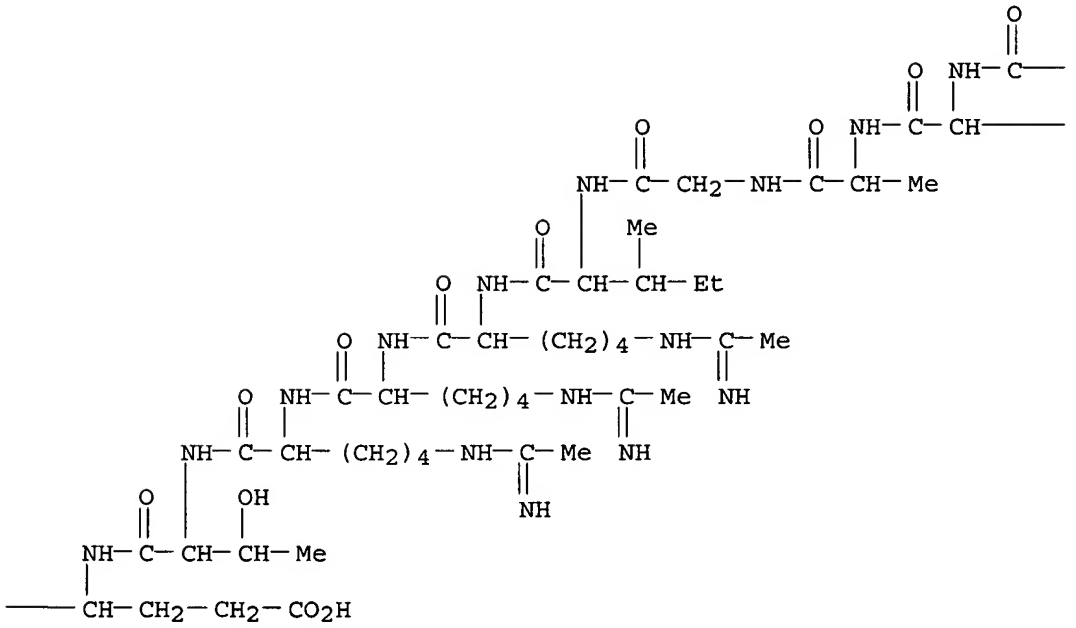

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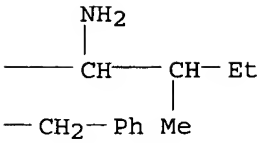

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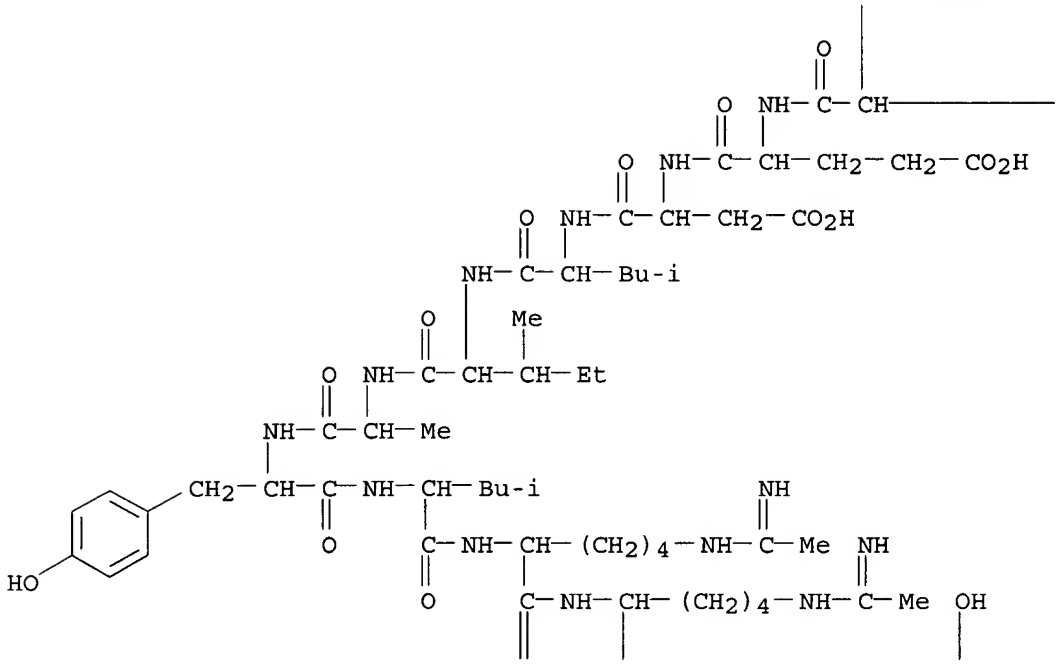

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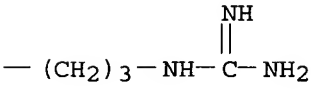

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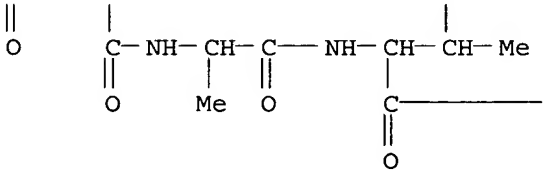

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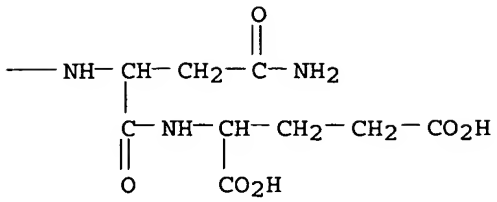
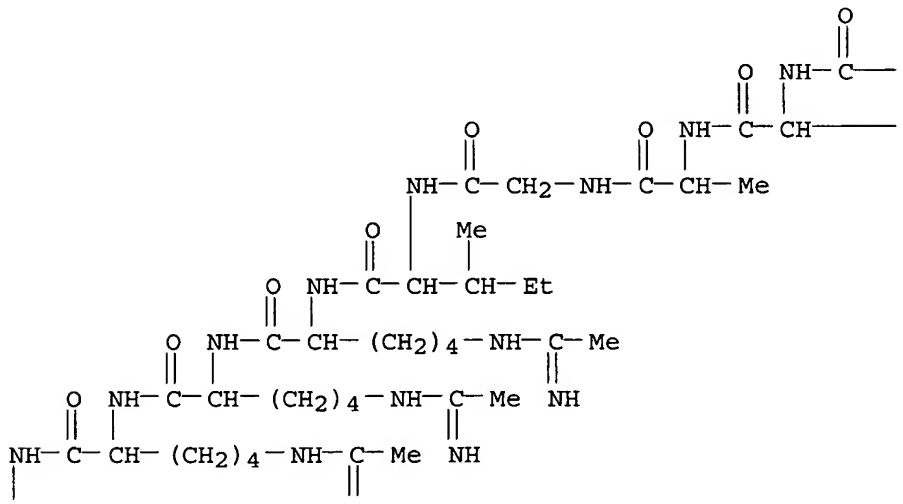


IT **70291-16-6P 70291-17-7P 70291-18-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 70291-16-6 HCAPLUS
CN L-Glutamic acid, S-[(acetylamino)methyl]-L-cysteinyl-L-methionyl-L-isoleucyl-L-phenylalanyl-L-alanylglycyl-L-isoleucyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-L-threonyl-L-α-glutamyl-L-arginyl-L-α-glutamyl-L-α-aspartyl-L-leucyl-L-isoleucyl-L-alanyl-L-tyrosyl-L-leucyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-L-alanyl-L-threonyl-L-asparaginyl- (9CI) (CA INDEX NAME)

PAGE 1-B



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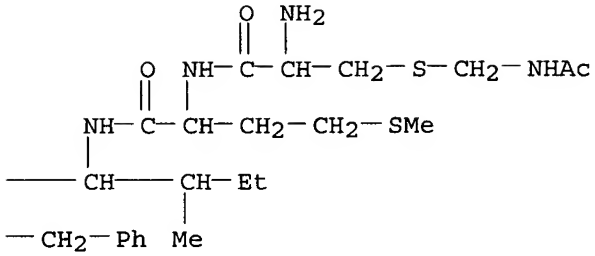

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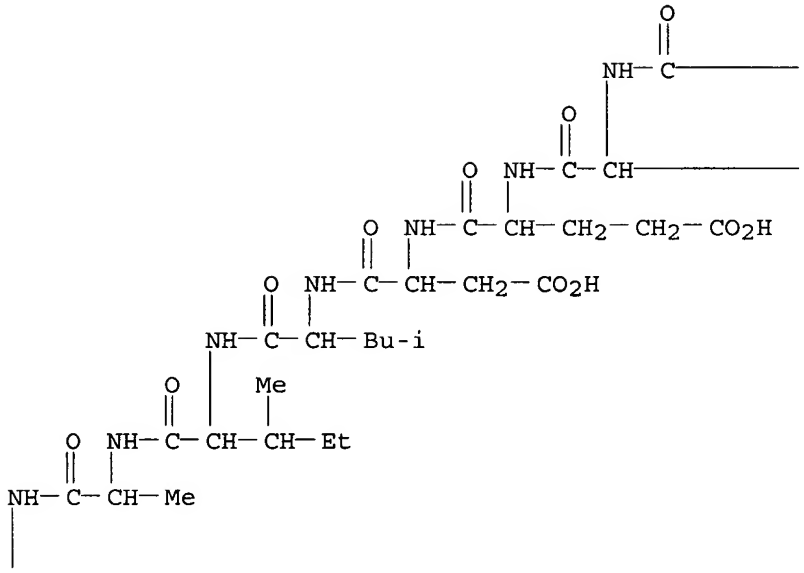

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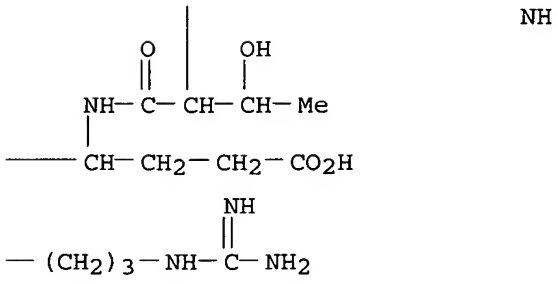

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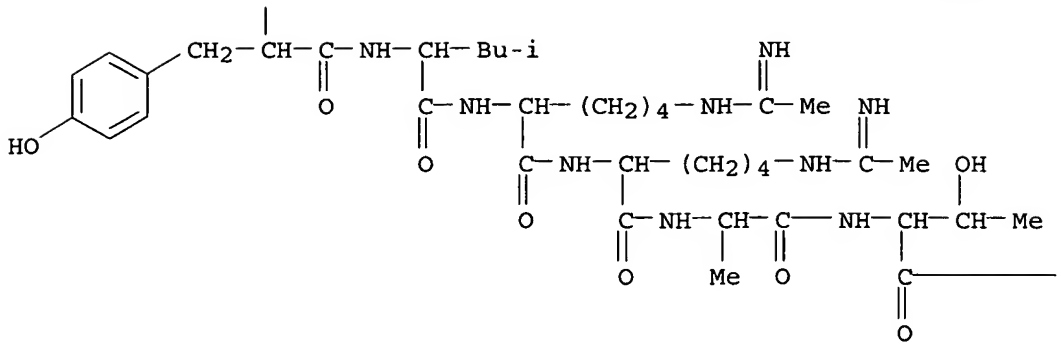

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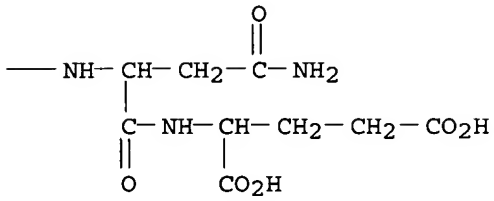
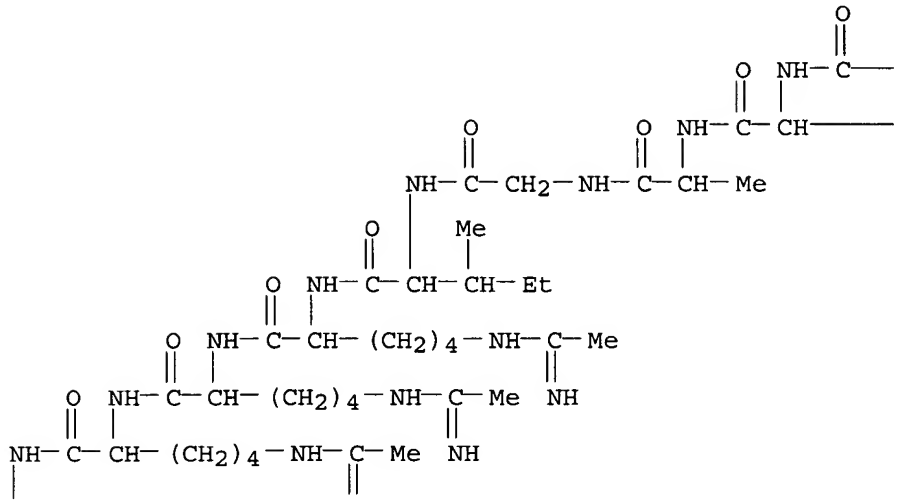


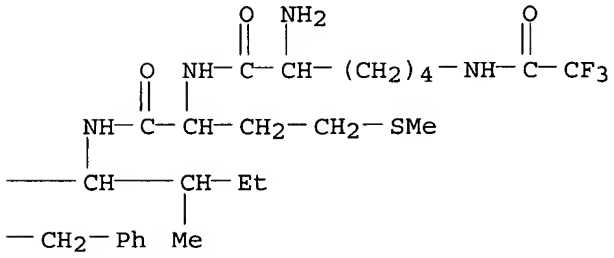
RN 70291-17-7 HCAPLUS

CN L-Glutamic acid, N6-(trifluoroacetyl)-L-lysyl-L-methionyl-L-isoleucyl-L-phenylalanyl-L-alanylglycyl-L-isoleucyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-L-threonyl-L-α-glutamyl-L-arginyl-L-α-glutamyl-L-α-aspartyl-L-leucyl-L-isoleucyl-L-alanyl-L-tyrosyl-L-leucyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-L-alanyl-L-threonyl-L-asparaginyl- (9CI) (CA INDEX NAME)

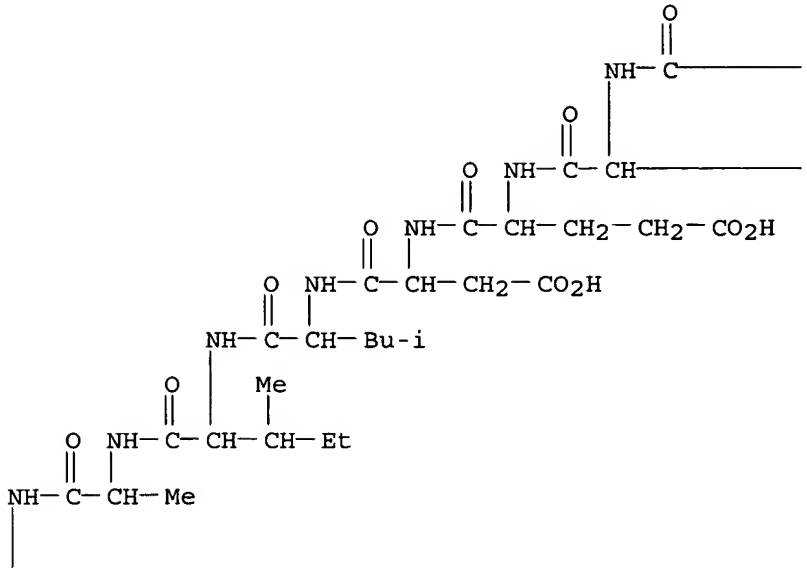
PAGE 1-B



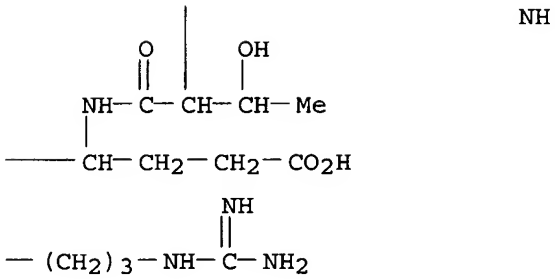
PAGE 1-C



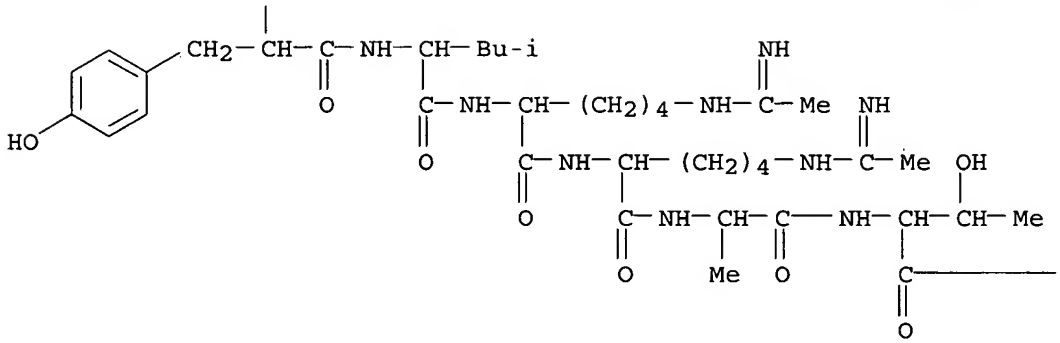
PAGE 2-A



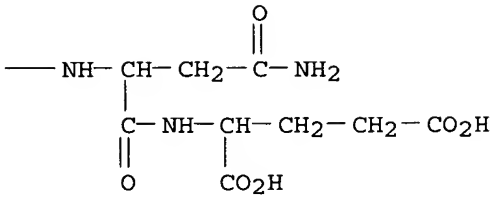
PAGE 2-B



PAGE 3-A



PAGE 3-B



RN 70291-18-8 HCAPLUS
CN L-Glutamic acid, N6-(2,4-dinitrophenyl)-L-lysyl-L-methionyl-L-isoleucyl-L-phenylalanyl-L-alanylglycyl-L-isoleucyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-L-threonyl-L-α-glutamyl-L-arginyl-L-α-glutamyl-L-α-aspartyl-L-leucyl-L-isoleucyl-L-alanyl-L-tyrosyl-L-leucyl-N6-(1-iminoethyl)-L-lysyl-N6-(1-iminoethyl)-L-lysyl-L-alanyl-L-threonyl-L-asparaginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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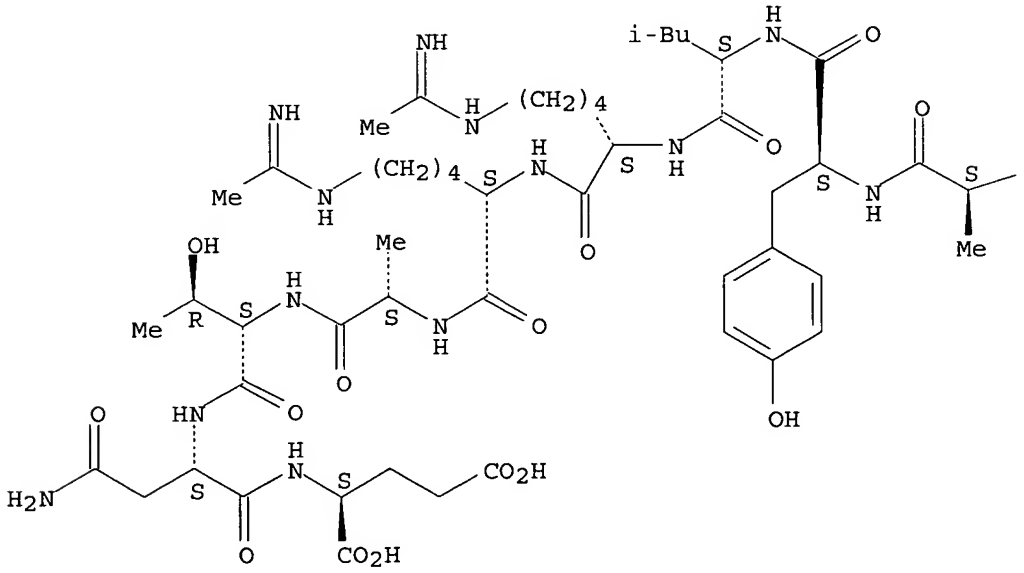
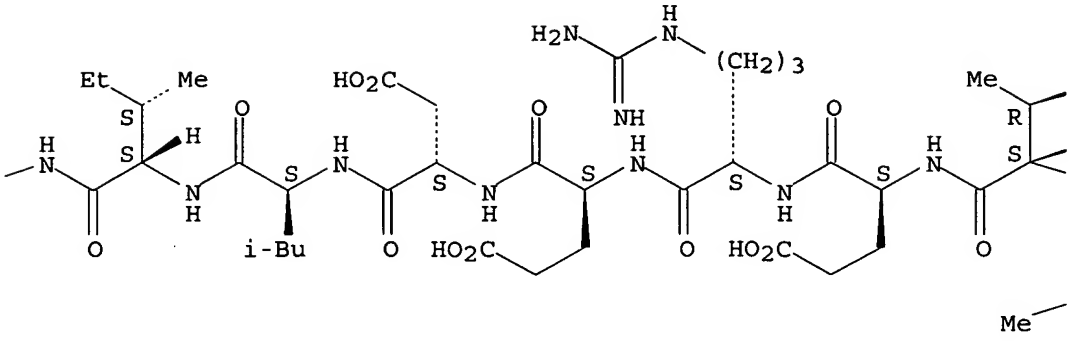


PAGE 1-B



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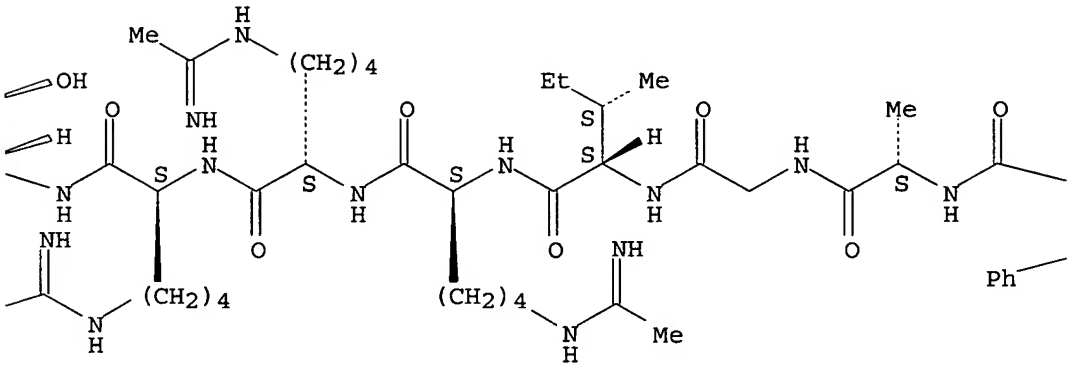
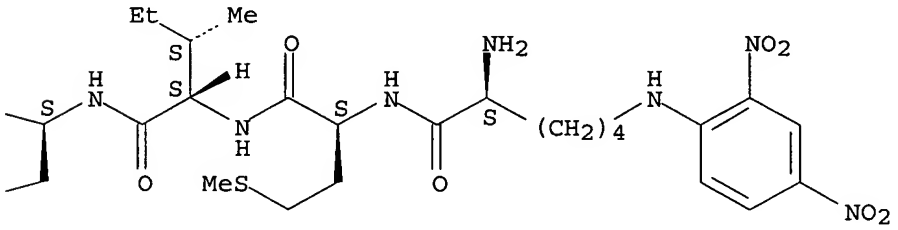
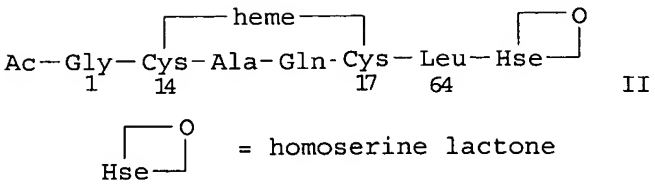


PAGE 1-D



L23 ANSWER 72 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:138196 HCAPLUS
DOCUMENT NUMBER: 90:138196
TITLE: Semisynthesis of [HSE65] cytochrome c
AUTHOR(S): Boon, P. J.; Tesser, G. I.; Nivard, R. J. F.
CORPORATE SOURCE: Dep. Org. Chem., Catholic Univ., Nijmegen, Neth.
SOURCE: Semisynth. Pept. Proteins, Pap. Int. Meet. Protein Semisynth. (1978), Meeting Date 1977, 115-26.

Editor(s): **Offord, R. E.; Di Bello, C.**
Academic: London, Engl.
CODEN: 39MMAW
DOCUMENT TYPE: Conference
LANGUAGE: English
GI



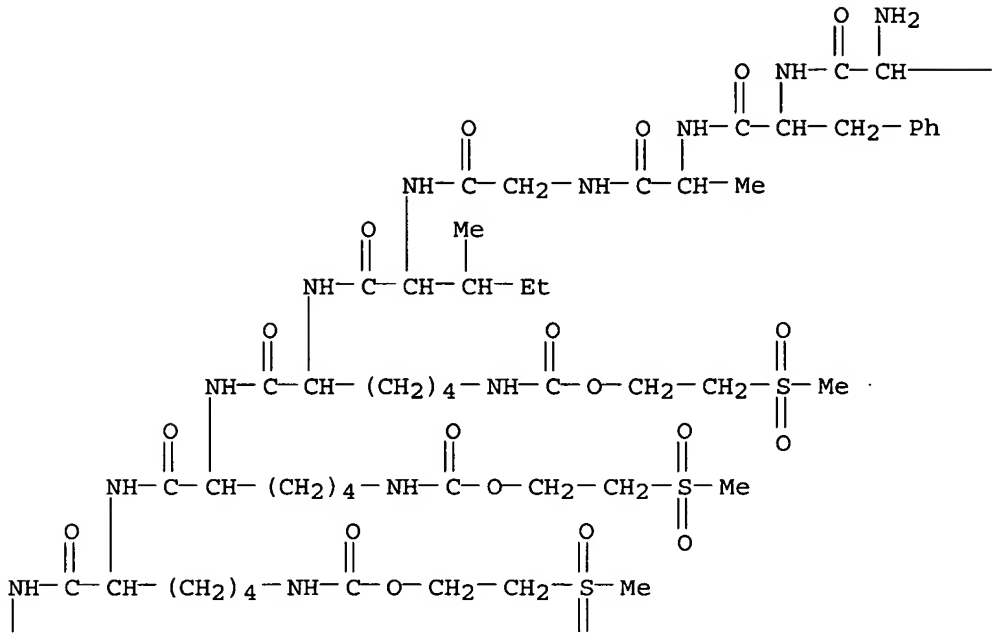
AB Horse heart cytochrome c (I) was cleaved with BrCN to give heme-containing fragment 1-65 II, which was coupled with cytochrome c fragment H-(66-104)-OH (III) to give the title compound I was Nε-acylated with Msc-OSu (Msc = MeSO2CH2CH2O2C, Su = succinimido) to give the Nε-nonadeca-Msc derivative, which was cleaved with BrCN to give Nε-penta-Msc cytochrome c fragment 81-104, which was coupled with BOC-Met-OSu (BOC = Me3CO2C) and then BOC-deblocked to give Nε-penta-Msc cytochrome c fragment 80-104 (IV). Msc-Glu-Tyr-Leu-Glu-Asn-Pro-Lys(Msc)-Lys(Msc)-Tyr-Ile-Pro-NNH2 (fragment 66-76) was prepared by conventional peptide couplings and coupled to H-Gly-Thr-Lys(Msc)-NHNHBOC (fragment 77-79) to give protected fragment 66-79, which was BOC-deblocked and coupled to IV by the azide method to give Msc-protected cytochrome c fragment 66-104. The latter was Msc-deblocked to give III.

IT **69630-95-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with methionine derivative)

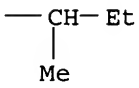
RN 69630-95-1 HCAPLUS

CN L-Glutamic acid, L-isoleucyl-L-phenylalanyl-L-alanylglycyl-L-isoleucyl-N6-[[2-(methylsulfonyl)ethoxy]carbonyl]-L-lysyl-N6-[[2-(methylsulfonyl)ethoxy]carbonyl]-L-lysyl-N6-[[2-(methylsulfonyl)ethoxy]carbonyl]-L-lysyl-L-threonyl-L-α-glutamyl-L-arginyl-L-α-glutamyl-L-α-aspartyl-L-leucyl-L-isoleucyl-L-alanyl-L-tyrosyl-L-leucyl-N6-[[2-(methylsulfonyl)ethoxy]carbonyl]-L-lysyl-N6-[[2-(methylsulfonyl)ethoxy]carbonyl]-L-lysyl-L-alanyl-L-threonyl-L-asparaginyl- (9CI) (CA INDEX NAME)

PAGE 1-B



PAGE 1-C



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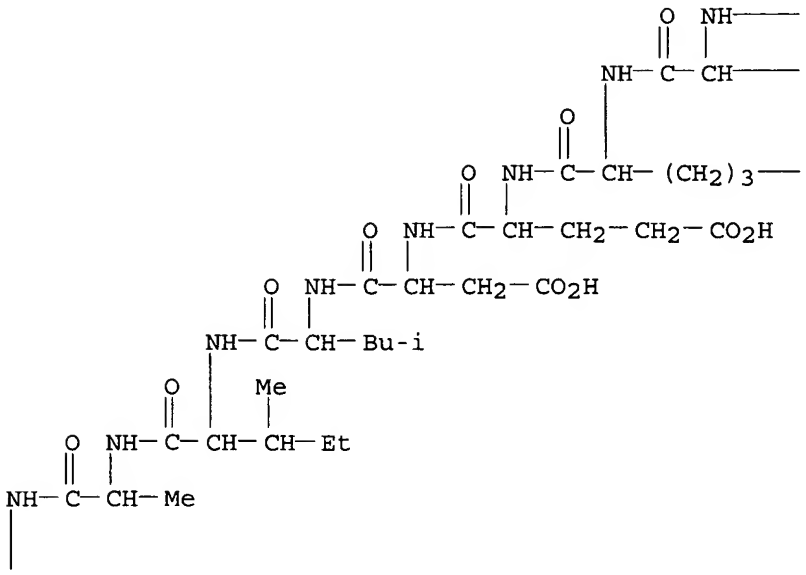
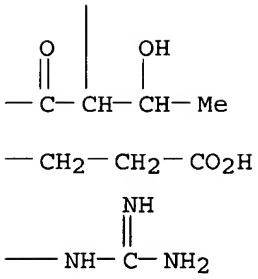


PAGE 2-B



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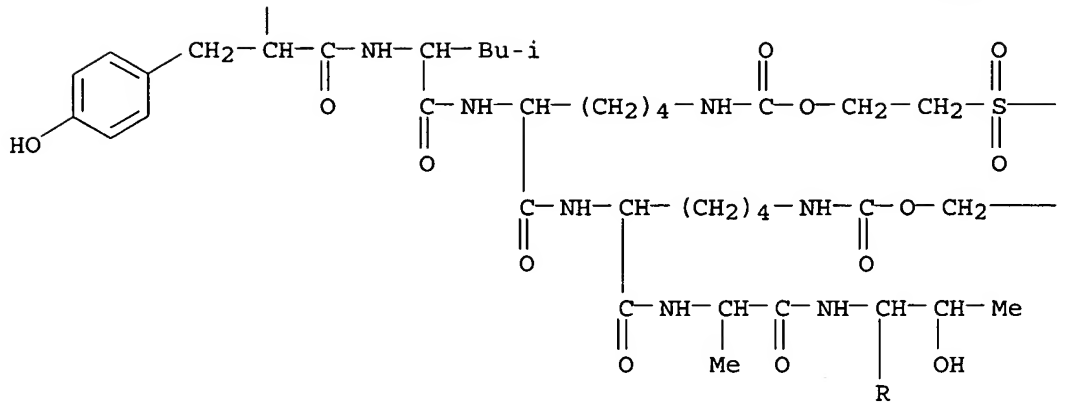

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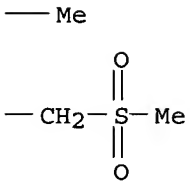

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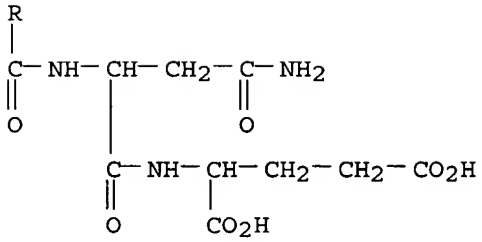

L23 ANSWER 73 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1979:104348 HCAPLUS
DOCUMENT NUMBER: 90:104348
TITLE: Structural analysis of semisynthetic products by computer-controlled mass-spectrometry directly coupled to gas-liquid chromatography of peptides
AUTHOR(S): **Rose, K.**; Priddle, J. D.
CORPORATE SOURCE: Dep. Zool., Univ. Oxford, Oxford, UK
SOURCE: Semisynth. Pept. Proteins, Pap. Int. Meet. Protein Semisynth. (1978), Meeting Date 1977, 387-95. Editor(s): **Offord, R. E.; Di Bello, C.** Academic: London, Engl.

CODEN: 39MMAW
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The title anal. was discussed and applied to elastase digests of insulin B chain and semisynthetic [Phe[13C]1]-insulin B chain.

L23 ANSWER 74 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:503058 HCAPLUS
DOCUMENT NUMBER: 89:103058
TITLE: Amino acid sequence determination by direct e.i./c.i. mass spectrometry of N-acyl; N,O-permethylated oligopeptides separated by gas chromatography
AUTHOR(S): Priddle, J. D.; **Rose, Keith; Offord, R. E.**
CORPORATE SOURCE: Dep. Zool., Univ. Oxford, Oxford, UK
SOURCE: Advances in Mass Spectrometry (1978), 7B, 1502-5
CODEN: AMSPAH; ISSN: 0568-000X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The separation of N-acyl N,O-permethylated peptide by gas chromatog., followed by the determination of their amino acid sequence using chemical ionization (c.i.)/electron impact (e.i.) mass spectrometry, is discussed. The volatility of peptides and their derivs. of 4 or 5 residues in length is discussed, and potential methods for derivatization of arginine and cysteine are examined

L23 ANSWER 75 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1977:135743 HCAPLUS
DOCUMENT NUMBER: 86:135743
TITLE: Direct sequencing of permethylated peptides by gas chromatography-mass spectrometry using electron impact and chemical ionization
AUTHOR(S): Priddle, J. D.; **Rose, Keith; Offord, R. E.**
CORPORATE SOURCE: Lab. Mol. Biophys., Univ. Oxford, Oxford, UK
SOURCE: Adv. Mass Spectrom. Biochem. Med. (1977), 2, 477-85
CODEN: AMSMDB
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A gas chromatograph was used to sep. O,N-permethylated oligoeptides (N-acetylated with both the acetyl and trifluoroacetyl groups), and a mass spectrometer was used to obtain their sequences. A prototype organic version of the Micromass 30 mass spectrometer (VG-Organic Ltd.) was used with a dual electron impact-chemical ionization (EI-CI) source in conjuction with a Pye 104 gas chromatograph. Representative scans of peptides, analyzed by the decribed procedures, are presented.

L23 ANSWER 76 OF 76 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1977:27368 HCAPLUS
DOCUMENT NUMBER: 86:27368
TITLE: The separation and sequencing of permethylated peptides by mass spectrometry directly coupled to gas-liquid chromatography
AUTHOR(S): Priddle, J. D.; **Rose, Keith; Offord, R. E.**
CORPORATE SOURCE: Dep. Zool., Univ. Oxford, Oxford, UK
SOURCE: Biochemical Journal (1976), 157(3), 777-80
CODEN: BIJOAK; ISSN: 0264-6021
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Permethylated acetyl- and trifluoro-acetyl-peptides were separated and sequenced in a single operation by gas.-liquid chromatog. coupled to mass spectrometry. Fragmentation was induced by electron impact and chemical ionization, the latter being the more sensitive method. Peptide derivs. of mol. weight at least 750 were accessible to the technique. The application of the method to the determination of the primary sequence of proteins is discussed.

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